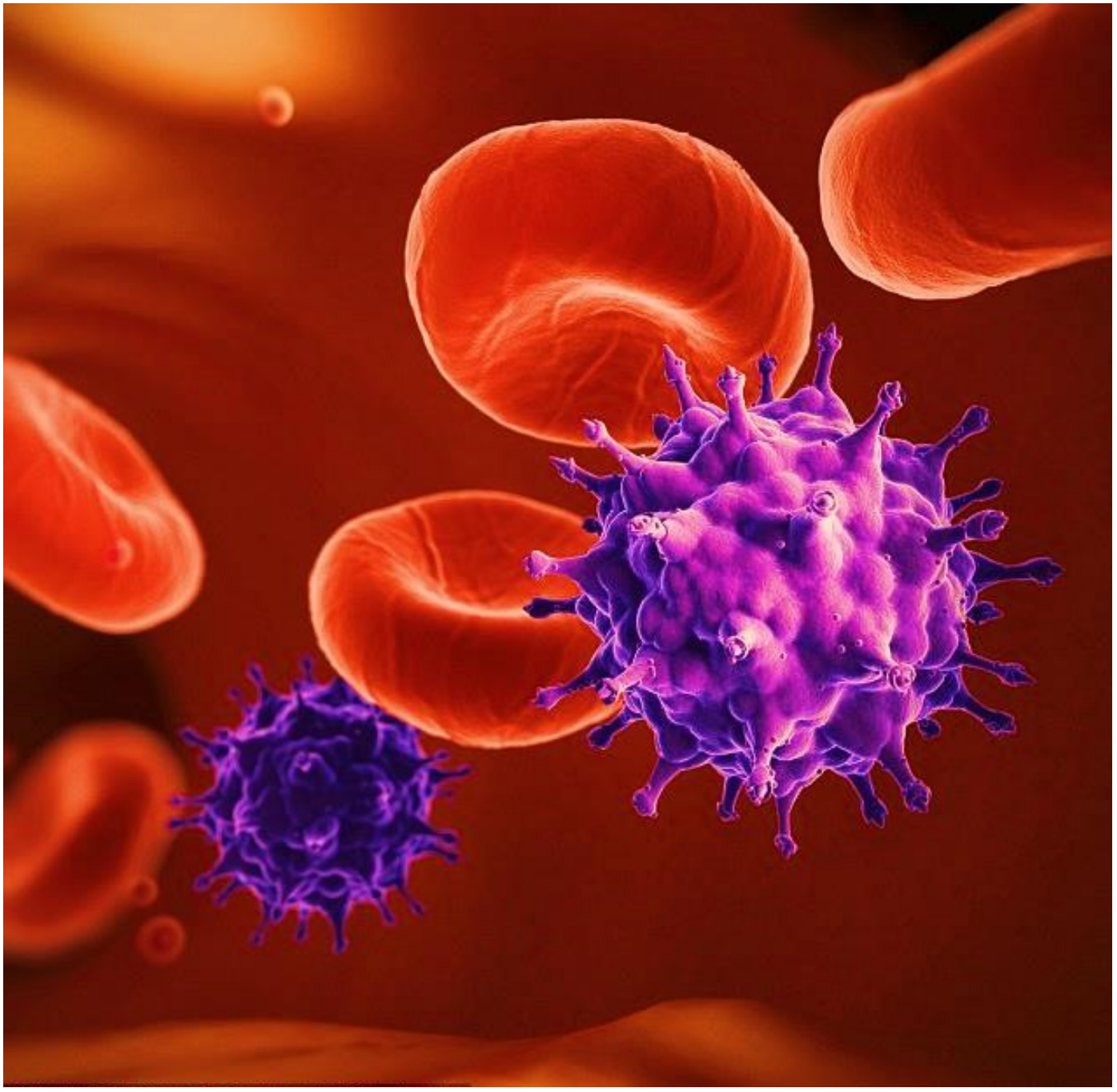
INFECTIOUS DISEASES



Dr. Osama Alagamawy

وَقُلِ اعْمَلُواْ فَسَيَرَى اللّهُ عَمَلَكُمْ وَرَسُولُهُ وَالْمُؤْمِنُونَ وَسَتُرَدُّونَ إِلَى عَالِمِ الْغَيْبِ وَالشَّهَادَةِ

فَيُنَبِّئُكُم بِمَا كُنتُمْ تَعْمَلُون ۝ (التوبة-105)

Say, Work righteousness; GOD will see your work, and so will His messenger and the believers. Ultimately, you will be returned to the Knower of all secrets and declarations, then He will inform you of everything you had done.

Al-Tawba Verse No: 105

Dedication

To the soul of my mother

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INTRODUCTION

Despite decades of dramatic progress in their treatment & prevention, infectious diseases remain a major cause of death & are responsible for worsening the living conditions of many millions people around the world. Infections frequently challenge the clinician's diagnostic skill. Many factors affect the likelihood of acquiring infection ẃ include, host, environmental & microbial factors, & environmental factors. For any infectious process to occur, the parasite & the host must first encounter each other. Factors such as geography, environment disease vectors & host behavior thus influence the likelihood of infection. Many host fac-tors as age, immunization, prior illness, nutritional status, pregnancy, coexisting illnesses & emotional status all have some impact on the risk of infection after exposure to particular pathogen. Medical care itself can ⇧ the pt's risk of acquiring an infection ẃ can occur in several ways; either through contact é the pathogen during hospitalization or through injections, surgical incisions, via mucosal surfaces by ETT or bladder catheters, or through introduction of foreign bodies, or through alteration of the natural flora é antibiotics, or through Rx é suppressive drugs as steroids. Infection involves complicated interaction between parasites & host. In most cases a pathogenic process consisting of several steps is required for the development of infection. Since the competent host has a complex series of defense mechanisms to prevent infection, the successful parasite must utilize specific strategies at each of these steps. The specific strategies used by bacteria, viruses & parasites have some similarities, but the details are unique not only for each class of organism but also for individual species in each class.

Definition

Infection: when a germ causes a disease. Is a condition that is caused by a multiplication of an infectious agent in the body.

Contamination: is the presence of infectious microorganisms in or on the body, environmental surfaces, articles of clothing, food, or water.

Contagious: when germs can be spread to others

Infectious: capable of causing an infection

Communicable: can be transmitted to others

Microbial virulence strategies

Microbes have developed variety of strategies for escaping immunity e.g. some organisms elaborate toxins/enzymes that facilitate the invasion of the host & often responsible for the disease state & many bacteria are encapsulated é polysaccharides that allow them to invade & deposit in the absence of specific antibodies.

Immune response

Is a defensive mechanism developed by the host for recognizing & responding to microorganisms. Is divided into 2 major classes:-

(1) Natural immunity: is the 1st line of defense, serves to protect the host éout prior exposure to the infectious agent. This immune response is nonspecific & has no memory. Examples of natural immunity include; intact skin & mm, cilia-ry function, phagocytosis by macrophages & neutrophils &complement system.

(2) Acquired immunity: specific immune mechanism developed against particul-lar organism. It takes time to develop & it has long standing memory and has 2 arms:-

a) Cellular immunity: comprising T-lymphocytes, & natural killer cells.

b) Humeral: comprises of B-Lymphocytes & antibodies produced by plasma cells.

Normal Micro flora & its importance

- Prevent the growth of pathogens.
- Stimulate the immune system to produce antibodies that cross-react with invading pathogens.
- Aid in digestion of cellulose in ruminants.
- Produce essential nutrients.

Types of Pathogens

1. Bacteria

- Often need to be treated with antibiotics
- Organism is larger than a virus.
- Can survive in or out of the body.

Include;

1. Gram positive: Streptococcus pyogenes, Staphylococcus aureus, Bacillus anthracis, Clostridium tetani .

2. Gram negative: Neisseria, Salmonella, shigella, E. coli, Yersinia pestis, Vibrio cholera

3. Acid-Fast e.g. Mycobacteria

2. Viruses

- Microscopic organism, are pieces of DNA or RNA surrounded by protein coat.
- May be encapsulated e.g. HIV, HBV, measles, mumps, influenza, rabies, Or non-encapsulated e.g.adenoviruses, HPV, Polio.

- Can grow or reproduce only in living cells with limited ability to survive outside of the body.

3. Fungus

Often on surfaces of body and can be treated with creams or oral medication

Organisms that get their nutrition from other living organisms or dead organic matter e.g. yeasts, molds, mildew, thrush, ringworm, and yeast diaper rash.

4. Parasite

- Single or multicellular organism.
- Lives on or in another living organism.
- Often need to be treated with antiparasitic medications
- Examples are tapeworm, louse, mite, pinworm, and giardia.

Virulent Factors: for all pathogens there is an infective dose and a lethal dose. The virulent factors that confer pathogenicity include;

- Pili that facilitate attachment.
- Capsules that interfere with phagocytosis.
- Endotoxins.
- Proteases that break down antibodies.
- Ability to vary antigens to evade antibodies.

Bacterial Pathogenesis

- Toxin production. Toxins fall into two categories; Exotoxins and Endotoxins.

- Invasiveness, where bacteria grow to large numbers locally and produce enzymes that damage host tissues.

Exotoxins: Heat labile (60-100 ^{0}C for 30 mins) proteins produced and **released** by

both gram positive and gram negative bacteria. Produced by bacteria such as *Clostridium (neurotoxins)* and *Bacillus (enterotoxin) (+)* and *E. coli* and *Vibrio (enterotoxin) (-).*

Endotoxins: are heat stable (100 ^{0}C for 1 hr), lipopolysaccharide produced only by gram negative bacteria e.g. Salmonella. They remain attached to cell wall. Cause fever and shock and is of lower toxicity compared to exotoxins.

Incubation period

for common diseases, can be remembered as follow:

- DICES: 1-7 days; Diphtheria, Influenza, Cytomegalovirus, Erysipelas, Scarlet fever, Herpes simplex.
- TP MEWs: 1-2 wks; Tetanus, Polio, Measles, Enterica (typhoid), Whooping cough.
- CRUMPs: 2-3 wks; Chicken pox, Rubella (German measles), Roseola, Mumps.

Order of appearance of rash

Very: day 1 Varicella (chicken pox, Herpes).

Sick: day 2 Scarlet fever.

People: day 3 Poxvirus.

Must: day 4 Measles.

Take: day 5 Enterica (Typhoid).

Entire: day 6 Typhus.

Rest: day 7 Relapsing fever.

Isolation period for common contagious infections

- Measles: 4 days before until 5 days after rash appears.
- German measles: 7 days before until 5 days after rash appear.
- Chickenpox: 5 days before rash until all sores have crusts (5-7 days).
- Roseola: from onset of fever until rash is gone (2 days).
- Fifth disease: (Erythema infectiosum): 7 days before rash until rash begins.
- Mumps: 5 days before swelling until swelling gone (7 days).
- Whooping cough: onset of runny nose until 5 days on antibiotic.
- Diphtheria: onset of sore throat until 4 days on antibiotic.
- Infectious mononucleosis: onset of fever until fever is gone (7 days).
- Scarlet fever: onset of fever or rash until 24 hrs on antibiotic.
- Meningitis: onset of symptoms & for 1 to 2 wks.
- Bronchiolitis: onset of cough until 7 days.
- Influenza: onset of runny nose until fever is gone.
- Croup (viral): onset of cough - stridor - until fever is gone.
- Tuberculosis: 2 wks on drugs (most childhood TB not contagious).

Causes of Fever with Rash

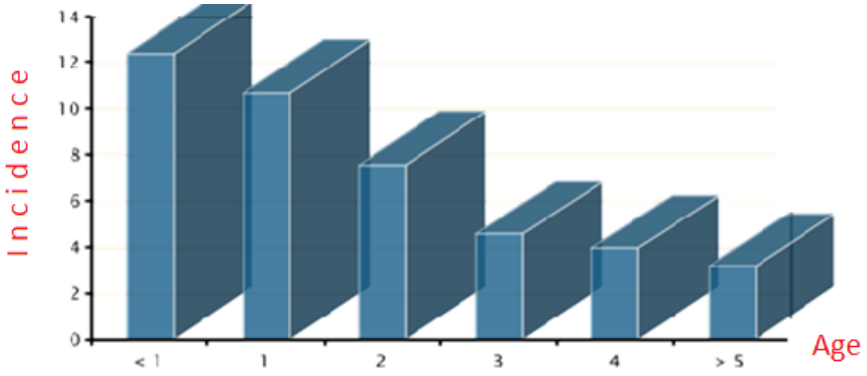
- Chicken pox: polymorphic, centripetal rash.
- Measles: monomorphic, centrifugal, kopliks spots.
- German measles: monomorphic, centrifugal.
- Fifth disease: slapped check rash.
- Roseola infantum: papular in trunk, rapidly spread to whole body.
- Kawasaki disease: papular & plotchy rash.

- Meningococcal meningitis: reddish to purple skin rash in whole body.
- Typhoid fever: rose spots on 5th day on the trunk.
- Endocarditis: petechial or ecchymotic generalized rash, Subconjunctival Hge, soft palate petechiae, Hge within nail bed (splinter Hge), painful SC nodes on palm (Osler's)

Characters of infection in the Early Childhood

- Sick more often
- Illnesses last longer
- More ear infections & are more likely to have tympanostomy tubes placed.
- More antibiotic-resistant bacterial infections

Annual Illness Incidence in the Early Childhood



The incidence of illness decreases from 12 per year to 4 per year by the time the child is 5 year old. 90% of infections are mild, self-limited& require no treatment

Why Children are more Vulnerable to Infectious Diseases?

Reasons why children are more vulnerable to infectious diseases include:

- Frequent hand-to-mouth behaviors.
- Still learning appropriate hygiene skills (keeping fingers out of nose, covering coughs, proper hand washing, etc)

- Some children may not be fully immunized, such as young infants.
- Children have close physical contact/do not practice much social distancing

Who is Most Vulnerable to Infection?

- Young infants are more susceptible because their immune systems are immature and don't have a lot of defenses (antibodies) built up yet. Some immunity is received from the mother through the placenta and some can be passed through breast milk, but it is still less than adults have.
- Children with special health care needs, including equipment in bodies: foreign bodies like metal devices can carry or capture bacteria, even if they were sterile when the device was placed. Devices like catheters can also carry bacteria even if the catheter is sterile and good cleaning procedures are followed.
- Children with impaired immune systems, including HIV/AIDS, chemotherapy, genetic conditions, transplants, or high-dose steroid therapy for longer periods.
- Pregnant women are not necessarily more susceptible themselves, but they can pass on certain infections to the fetus if the mother is not immune to the disease.

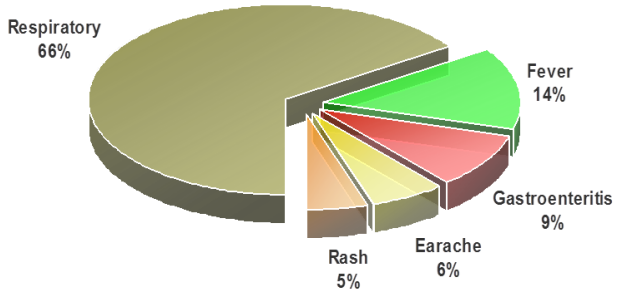
Symptoms of Infectious Diseases

- Cough. • Runny nose and/or congestion. • Difficult or noisy breathing. •Vomiting, nausea, or stomachache. •Diarrhea. •Rash. •Itching. •Drainage or irritation of eye or other infected body part. • Fever. • Aches or pains: Sore throat, earache, headache, body ache. • Mouth sores. • Swollen glands. • Behavior changes.

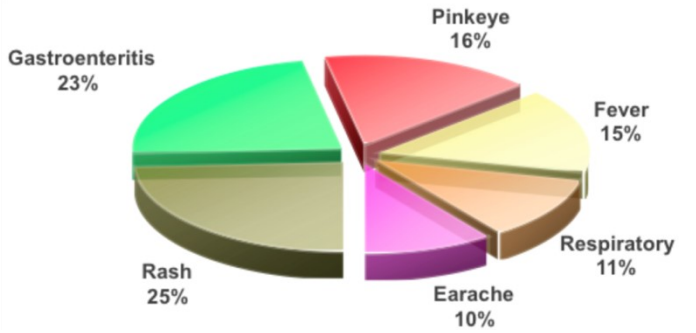
Common Symptoms Reported in Early Education Settings

- Respiratory symptoms (cough, congestion, runny nose) are the most common symptoms seen in early education settings. They comprise 66% of the total.

- The second most common is fever (14%).
- The third most common is gastrointestinal (vomiting and diarrhea) (9%).



Common causes causing absence from school



Although respiratory symptoms are the most common (65%),they only cause 11% of the absences. Symptoms that are more likely to cause absence are rash, gastro-intestinal (vomiting and diarrhea), and pinkeye. The difference between which symptoms are common and which ones cause absence probably has to do with exclusion policies. New vaccines like rotovirus and pneumococcal may change these statistics.

How Infectious Diseases Spread

- Respiratory droplets. Some germs from the respiratory tract can spread by breathing the air close to someone who has coughed or sneezed. Most germs from the respiratory tract, however, are spread when a person's hands are contaminated by touching moist secretions from an infected person's nose, eye, or mouth, and then touching his or her own eyes, nose, or mouth.
- Fecal-Oral: Germs spread from the feces to the mouth, usually via the hands.

With typical diaper changing and mouthing behaviors, hands, floors, toilet and faucet handles, diaper changing areas, toys, and countertops frequently are contaminated with fecal matter.

- Direct contact: Touching the person or the object that has live germs on it.

Examples are: hands mix germs into modeling compound, and mucus is mouthed onto toys.

- Body fluids: Blood, urine, and saliva have germs that touch someone and enter the body through open skin, the mouth, nose, or other mucous membranes.
- Insects: Can harbor germs that can be passed, especially if the insects pierce the skin.
- Placental-fetal route

Laboratory diagnosis

Diagnosis of infections requires the demonstration of organism either;

1. Direct microscopic visualization of pathogens in clinical material or the growth of microorganisms in culture.

2. Indirect e.g. antibody/serology test, of viral, bacterial, mycotic, or parasitic agents in fluids, tissues, or excreta of the host.

Treatment

Optimal Rx for infectious diseases requires broad knowledge of medicine & careful clinical judgment. Life threatening infections as bacterial meningitis/sepsis require urgent initiation of Rx often before a specific infective organism identified. Antimicrobial must be chosen empirically & must be against the range of potential infectious agents consistent é the clinical condition.

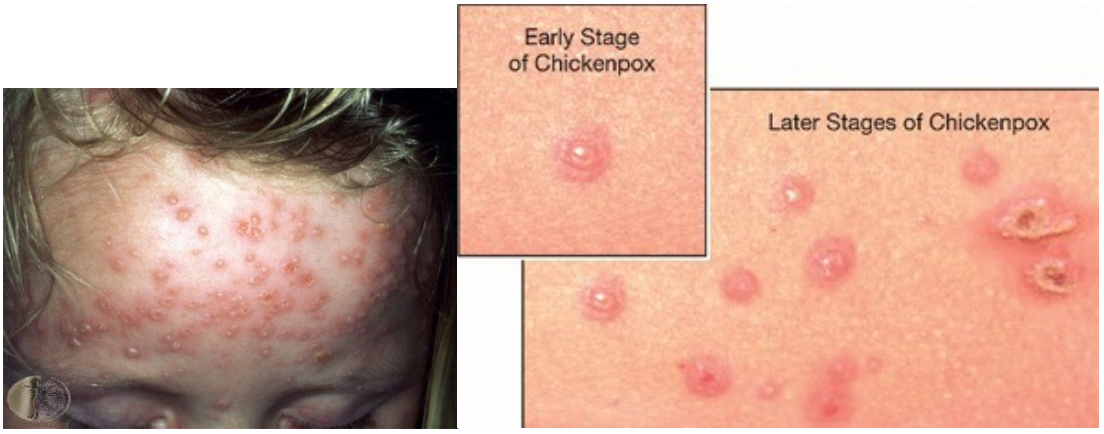
Immunoglobulins

Used in case of;

- Kawasaki disease.
- Chicken pox within 3 days from exposure.
- AIDS.
- ITP.

Amp 2 ml, 0.2 ml/Kg IV/IM for 3 successive days.

CHICKEN POX



Caused by Varicella-Zoster Virus (also known as VARICELLA). Highly contagious. Most people infected by age 5 years. Immunity ⇧ ē age. Outbreaks usually winter /spring. Epidemics every 2-5 yrs. Spreads via respiratory tract. The IP 2-3 wks. Infective from 5 days before rash, until crusts fall off. Days 1 & 2 are the most infective.

Clinical Picture

The virus first infects mucous membrane of URT. Viral proliferation occurs in LNs for 2-4 days after the initial infection. 4-6 days after initial infection, virus enters blood stream, this is followed by a second round of replication in body's organs especially in spleen & liver. The prodromal stage is short, 1 day of fever, malaise & URTI. The Rash is itchy & scratchy, centripetal & polymorphic, start in abdomen, may be one spot in face, or thumb, then next day it cover the whole body.

Complications

- Secondary infection (scratching).
- Secondary Bacterial infection especially Group A Streptococcal.
- Encephalitis.
- CNS-cerebellar ataxia, myelitis, vasculitis.
- Osteomyelitis.
- Sepsis.
- Otitis media.

Management

#Isolation until rash completely crusted.

#Keep skin clean by frequent baths or, once the fever has subsided, showers. Cool, wet compresses or tepid water baths help to relieve itching.

#Antihistamines may used to help relieve the itching.

#Acyclovir is used for severe infection involving the lungs or the brain & in persons ē a depressed immune system. Oral Acyclovir 200 mg, dose 15 mg/Kg/day ÷ 3 X 5 days.

Prevention

✵Children between 12-18 months should receive a dose of chickenpox vaccine, Varicella-zoster immune globulin.

✵Many countries have passed legislation requiring the chickenpox vaccine for child care & school entry.

✵Healthy children older than 13 & adults who have no history of chicken pox & have never been immunized against the disease, should be given the vaccine.

✵Contacts can be given within 3 days from exposure dose of hyperimnoglobulin 0.2 ml/Kg (amp 2 ml).

✵ Avoid pregnant women, neonates, immunocompromised.

MEASLES

Highly contagious viral illness. First described in 7th century. The IP 1-2 weeks. Affect age group 2-5 years. Its peak is Marsh. Infective 4 days before & 5 days after rash appears. Infective 5 days before & after rash.

Clinical picture

Severe manifestations of URTI; fever, cough, running nose, conjunctivitis for 3-5 days. Appearance of Kopliks spots on the third day opposite the lower first & second molars (one day before appearance of rash). Rash is monomorphic, centrifugal start in face. The temperature decline ē appearance of rash.

Investigations: measles specific antibodies IgM.

Complications

Diarrhea, otitis media, pneumonia, encephalitis

Management

- Symptomatic treatment.
- Isolation 5 days before until 5 days after rash appears.

GERMAN MEASLES

Rubella comes from the Latin words for “little red”. Creates dense groups of small skin rash. Produces swollen LNs, runny nose & fever. Spread through respiratory droplets from coughing & sneezing. Also spread through body secretions & excretions. The IP 2-3 wks. infection during pregnancy (1st TM) lead to; miscarriage, fetal death, premature delivery, or live birth ē congenital defects (CRS) ē its classic triad; Cataract, Cardiac abnormalities & Deafness..

Clinical picture

- Short prodromal stage 1-2 days.
- Mild fever, cough, running nose, enlarged tender posterior auricular LNs.
- Rash is monomorphic & centrifugal (start in neck & face).

Management

No specific therapy.

Isolation period is 7 days before until 5 days after rash appear.

Symptom-based treatment.

Immunoglobulin does not prevent rubella infection, only for pregnant woman who exposed to rubella, whom will not consider termination of pregnancy under any circumstances (IM immunoglobulin within 72 hrs of rubella exposure).

Prevention: rubella vaccine contains live attenuated rubella virus grown in human diploid cells, combined ē measles &rubella (MR) or measles, mumps & rubella (MMR) formulations, or tetravalent measles, mumps, rubella & varicella (MMRV) vaccine. One dose induces seroconversion in 95% of persons >1 yr of age.

FIFTH DISEASE

Fifth disease is a common childhood infection, caused by parovirus, its IP is 1-3 weeks. Most commonly affects young children & often occurs in several members of the family or school class. Infective from 14 days before & ceasing at the onset of the rash. No recommendation to keep away from school once well.

Clinical picture

Causing a slapped cheek appearance, rash appear first on face as if he is slapped in his face. The rash then spread to arms & chest as red spotty rash, continue for 1-3 weeks. 30% of cases have no symptoms. May associated ē fever, rash continue for 1-3 weeks. Once rash appear, the child will be not infective.

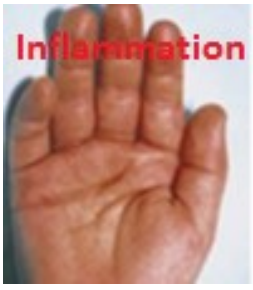
ROSEOLA INFANTUM

Caused by Herpes virus (HHV6 &7), also called 6th disease. Higher incidence during spring spring & fall months, the IP 5-15 days. Most adults excrete HHV-6 &7 in saliva & may ser-ve as primary sources for virus transmission to children. The prodromal period is usually asymptomatic; mild URI signs, mild cervical or less frequently occipital lymph nodes may be noted. Some chidren may have mild palpebral edema.Clinical illness is generaly heralded by high temparature ẃ persists for 3-7 days ; resolves abruptly. A rash appears within 12 - 24 hrs of fever resolution, rash appear as rose colored, distinctive on the trunk → to neck ,face, proximal extremities (centripetal, maculopapular). The rash fade in 1-3 days. Some childr-en may become irritable & anorexic. Seizures may occur in 15% of cases. Rhinorrhea, sore throat, abdominal pain, vomiting & diarrhea may be associated ē the disease. The characteristic enanthem consist of the soft palate &the base of the uvula. The enanthem may be present on the fourth day in 2/3 of pts ē roseola.

Diagnosis: Specific test for HHV 6-7. - Virus culture. - PCR. - Antigen detection

Management: no specific treatment. Antipyretics (never use aspirin). Paracetamol drops 100 mg, syrup 250 mg, supp 120mg, maximum dose 1200mg/D. Marcofen pediatic syrup or supp 100 mg, 1 X 2 for baby >6 months age. HHV-6 is inhibited by Ganciclovir (but not Acyclovir).

KAWASAKI DISEASE



A self-limited, diopathic multisystem disease characterized by vasculitis of small & medium blood vessels, including coronary arteries of unknown etiology ? viral, that predominantly affects children < 5 yrs age. The peak age onset is 9-11 months. It is now the most common cause of children acquired heart disease.

Epidemiology

Incidence in the UK is 8.1/100 000 children < 5 yrs old. In Japan its 220/100.000 children < 5 yrs old. It is over-represented in Asian & African-Americans. Seasonal variation- more cases in winter & spring but it can occurs throughout the year.

History of Kawasaki Disease

Original case observed by Kawasaki, January 1961, 4 yrs old boy, “diagnosis unknown”. Coronary artery thrombosis first recognized 1965 on autopsy of child previously diagnosed ē /MCOS. First Japanese report of 50 cases, 1967. First English language report from Dr. Kawasaki 1974, simultaneously recognized in Hawaii.

Diagnostic Criteria

✶Fever for at least 5 days & At least 4 of the following 5 features:-

①Changes in the extremities - oedema, erythema, desquamation.

②Polymorphous exanthema, usually truncal.

③Conjunctival injection.

④Erythema &/or fissuring of lips & oral cavity.

⑤Cervical lymphadenopathy.

✶Diffuse dilation of coronary arteries during the acute phase occurs in in 30-50% of pts. The aneurysms persist in 15%, while 50% regress to no observable lesion.

✶ECG changes; arrhythmias, abnormal Q waves, prolonged PR &/or QT intervals, low voltage, ST-T wave changes.

✶ECHO & CXR for CA`s aneurysm & cardiomegaly.

Management

Immunoglobulins IV or IM, Gama globulin 5 %, 2.5 mg/100 ml, 1 ml/Kg/day for 3 successive days to ⇩ the risk of coronary artery aneurysm.

No aspirin.

Plavix 75mg daily for long duration.

Corticosteroid: not recommended to use & only can prescribed when the therapeutic effect of IVIG is not satisfied, Prednisolone in a dose of 2 mg/kg, 2-4 wks, then gradual tapering.

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POLIO

Caused by Polio virus. Incubation period 1- 2 wks, characterized by selective affection of motor nerves, anterior horn cells of spinal cord. Any group of muscl-es can be affected as lower motor neuron lesion (loss of muscle tone, power, ref-lexes, absence of Babiniski sign, presence of fasciculations, intact sensation). May affect respiratory muscles. Bulbar palsy when affect brain medulla & cranial nerves 9, 10, 11, 12, resulting in dysphagia, dysphonia.

Clinical picture

Prodromal stage: URTI for few days, followed by paralytic stage, affected limb is painful at first but ē repeated passive movement pain subside. The sensation is intact. 2/3 of cases will have residual neurological seqelae.

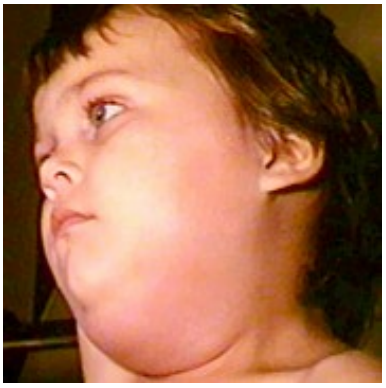
Investigations

- Isolation of virus from stool in prodromal stage, or blood in the paralytic stage.
- PCR. • Polio antibodies (IgM, IgG). • CSF: ⇧cells, ⇧ proteins & normal sugar.

Management

- Complete rest for 2 wks in the maximum functioning position of affected limb.
- Ventilator care in case of affection of respiratory muscles.
- Physiotherapy after the 2 wks.

MUMPS



Viral infection. The IP 2-3 wks, peak is in June, July, August, single attack cause permanent immunity. Mumps affect the salivary glands, especially the parotid, spread through airborne transmission of respiratory droplets by sneezing & coughing, also spread from direct contact ē saliva.

Clinical picture

Primary symptom is swollen checks. The swelling is elastic, painful, better seen than felt, at angle between mastoid process & mandibule, pushing ear lobule upward, stensen duct opposite the upper second molar teeth is red&edematous. Can also cause fever, headache & malaise may be presented or complicated by encephalitis or orchitis (common) or oophritis (rare).

Management

- Mouth hygiene care; Tantum Verde mouth wash 1 tsp as gargle 3-6 times daily, or Sulfa Buracyl 1 tsp over one cup of warm water gargle 3-6 times daily.
- Mumps is infective for 10 days after appearance of swelling.
- It is important to do audiogram after pt cure because it is commonly cause unilateral nerve deafness.
- It is Important to do urine analysis after cure as it may cause diabetes mellitus.

TONSILLITIS

Mainly a disease of childhood but is also seen in adults. May occur primarily as infection of the tonsils themselves or may secondarily occur as a result of URTI following viral infection

Organisms

- Beta-haemolytic streptococcus.
- Staphylococcus.
- Haemophilus influenza.
- Pneumococcus.
- The part played by viruses in acute tonsillitis is unknown.

Clinical picture

Common in cool rainy months, of sharp onset, painful swallowing, tender cervical LNs, if viral will be associated ē running nose cough, hoarseness, important sign of chronicity is the marked flush of the medial border of anterior faucial pillars. Quinsey is rare complication (peritonsilar abscess), pushing tonsil medially tow-ards uvula ass-ociated ē swollen soft palate.

Management

- Paracetamol drops 100 mg, syrup 250 mg, suppository 120 mg, maximum total daily dose 1200mg. Marcofen ped. suppository 100 mg, 1 X 2 for baby >6 months
- Augmentin syrup (β-lactamase Inhibitor), 156, 312, 457 mg, tab 612, amp 600 , 50 mg /Kg ÷3 X 5 days .
- Tonsillectomy in chronic cases, associated ē improve appetite, activities.

SCARLET FEVER



Group A B hemolytic streptococci, affect commonly school age children, 2-4 days post streptococcal pharyngitis.

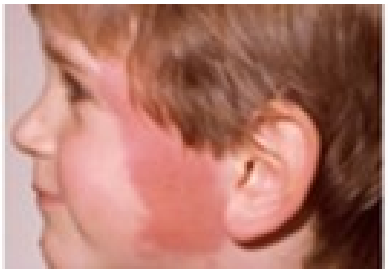
Clinical picture

Presented ē fever, headache, sore throat, white strawberry tongue, flushed face ē circumoral pallor, unwell, rash may extend to whole body, rough ‘ sand paper ’ skin, desquamation after 5/7 days, particularly soles & palms.

Investigations: ➢ Throat swab. ➢ ASO titer.

Management: Penicillin 10 days.

ERYSIPELAS




Cellulitis & Erysipelas are skin infections that develop as a result of bacterial entry via breaches in the skin barrier. Cellulitis & Erysipelas manifest as areas of skin erythema, edema & warmth. They differ in that erysipelas involves the upper dermis & superficial lymphatics, whereas cellulitis involves the deeper dermis & SC fat. Erysipelas is caused by strept pyogenes, or staph aureus , may be complicated by sepsis.

Erysipelas	Cellulitis
Abrupt onset ē fever	A low grade fever may be present ē a less abrupt onset
The skin is bright red	The skin is dull red
A spreading, hot, tender plaque ē well-defined border	The border is less well defined, fades into the surrounding skin
Vesicles & bullae may be present	No blisters

Management

Penicillin G ampule 1000.000 U, 100.000U/Kg/day ÷ 4 IV, for 2 wks. Flummox syrup 250 mg, cap 250, 500 mg, amp 1000 mg, IV/IM, 50-100 mg/ Kg ÷ 3 X 10 days (Amoxicillin + Flucloxacillin). Avil retard tab 1 X 1 daily. Reparil tab 1 X 3 daily (antioxidant, anti-inflammatory). Dermovate cream 1 X 2 daily (steroid).

IMPETIGO



Bacterial skin infection. Often called school sores, mostly affects children. Is quite contagious. Commonly staph Aureus or Group A Strep Pyogenes. Classically presented ē ruptured vesicles ē honey-colored crusting, may be bullous, more common in pre-existing ting skin disease, rapid spread. Commonly starts around face /mouth.

Management

During the infectious stage (while the impetigo is oozing or crusted); cover the affected areas, avoid close contact ē others, affected children must stay away from school until crusts have dried out, use of separate towels & flannels. Change & launder clothes & lin-en daily. Topical Fusidic Acid or oral Flucloxacillin; Flummox syrup 250 mg, capsule 500 mg, amp 1000 mg (in severe cases), dose 50-100 mg/Kg ÷ 3 for 5 days. Ectometherine ointment after warm bath & good rubbing of skin.

METHICILLIN-RESISTANT STAPHYLOCOCCUS AUREUS

MRSA is on the rise and MRSA exposure for EMTs and paramedics is greater than

for the general public. Type of staph bacteria resistant to common antibiotics. Traditionally associated è hospitals but now is epidemic of community-acquired MRSA. Multiplies rapidly causing many types of infection ranging from skin infections to septicemia and toxic shock syndrome. The best defense against MRSA is to wash your hands often, especially after contact è other people. Thorough washing è soap & water or alcohol hand disinfecting gels is effective against MRSA

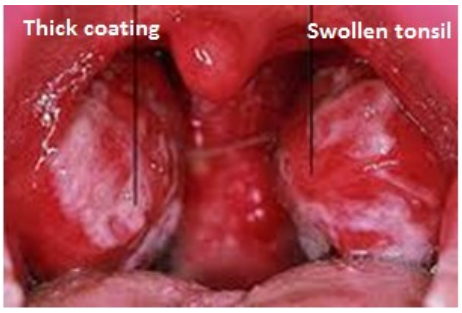
Transmission: found commonly on human skin, in nose & throat, less commonly, in colon &in urine. Can infect other tissues when skin or mucosal lining have been breached.

Occupational Exposure: can be spread through contact è pus from infected wound, skin-to-skin contact with infected person, & contact è objects such as towels, sheets, or clothing used by infected person.

Prehospital Presentation: Staph infections, including MRSA, generally start as small red bumps that resemble pimples, boils, or spider bites. Can quickly turn into deep, painful abscesses. Can also burrow deep into body, causing potentially life-threatening infections in bones, joints, surgical wounds, the bloodstream, heart valves, & lungs.

Prevention: best defense against MRSA – wash hands often, especially after contact with other people. Thorough washing with soap & water or alcohol hand disinfecting gels is effective against MRSA. Wear a gown when caring for patients with a known or suspected MRSA infection of the skin. In some cases MRSA is a respiratory infection. Patient has known or suspected MRSA skin infection & has a cough, or has MRSA respiratory infection, wear fitted mask. Put surgical or procedure mask on the patient if they can tolerate it.

INFECTIOUS MONONUCLEOSIS



Epstein Barr Virus, The IP 1-2 months, common in age 2-4 yrs & in adolescent.

Clinical picture

Marked inflammation & congestion of tonsils, fever continue for 2-4 wks, generalized lymphadenopathy in 90% of cases, hepatosplenomegaly in 50 % of cases, in addition to malaise & fatigue.

Investigations

- CBC: leucocytosis, >20.000/cm^3 mostly lymphocytes, atypical lymphocyte.
- Antibodies: IgM for EBV in acute illness, IgG for EBV in chronic illness.
- Paul Bunnel test: for a titer 1/200.
- Monospot test: positive.

Management: no specific treatment.

DIPHTHERIA

An acute toxic infection caused by Corynebacterium diphtheria & rarely toxigenic strains of Corynebacterium ulcerans. Aerobic,non-capsulated, non-spore forming

,mostly non-motile pleomorphic, gram +ve bacilli. Differentiation of C. Diphtheria from C. Ulcerans is based on urease activity, C. Ulcerans is urease +ve. There is 4 types of C. Diphtheria biotypes including; Mitis, Intermedius, Belfanti & Gravis. The differentiation is by colonial morphology, hemolysis &fermentation reaction.

Clinical picture

Pharyngeal (commonest), nasal or conjunctival, pt looks toxic, feverish, dirty white mem-brane over tonsil, gradually spread to anterior pillar, uvula & other tonsil, trial of removal result in underneath bleed.

Investigations

✡ Pharyngeal swab urgent for culture. ✡ CBC.

Management

Diphtheria antitoxin ½ IV, & ½ IM 20.000-80.000 U/day until complete recovery, after doing allergy test by diluting to conc. 1:100 - 1:1000, 0.1 ml, ID, observe for 1 hour for any local reaction, if sensitive use adsorbed purified toxoid, if not available do desensitization as follow;

0.1 mL 1/20 conc. + 0.05 ml adrenaline SC. After 30 min

0.1 mL 1/10 conc. + 0.05 ml adrenaline SC. After 30 min

0.01 ml full conc. + 0.05 ml adrenaline SC. After 30 min

0.1 mL full conc + 0.05 ml adrenaline SC. After 30 min

1/2 mL full conc + 0.05 ml adrenaline SC. After 30 min

Full dose IM ē the presence of adrenaline, decadron ready for use in case needed

Penicillin G 200.000U/Kg/day ÷ 4 for 10 days, or

Erythromycin 500 mg X 4, 50 mg/Kg/day ÷ 4 for 10 days in case of penicillin allergy. # Isolation until 3 throat swabs/day are negative.

OTITIS MEDIA

Peak is 6-12 months, 50% at age 3 years, 25 million visit per year to pediatricians for otitis media in USA, bacterial in origin in 60% of cases, viral 15% & nonspecific in 25% most bacterial infection are due to streptococcal pneumonia & Haemophilus influenza, common ē tonsillitis & URTI, postmortem examination of prematures shows 75% of them had otitis media.

Clinical picture

Fever not required for diagnosis, visualize the drum for loss of luster, presence of inflammation or dilated vessels. Check for swelling or tenderness behind ear pinna (over mastoid process) ẃ suggest mastoditis.

Secretory otitis media: lead to conductive deafness, common in age group 2-5yrs ,uni or bilateral, nerve conduction is better than air conduction. Treated ē nasal decongestant, antihistaminic & myringotomy ē no improvement, ventilation tube (grommet) ẃ extruded by itself.

Swimming pool otitis media: chemical irritation, lead to obstruction of Eustachian tube & ear pain, resolve within 1-2 wks, .Treated ē Otal drops, Oto calm drops ,anti-allergic syrup, in addition to antibiotic.

Acoustic neuroma: in adults presented ē loss of equilibrium & balance,associated ē nerve deafness & nystagmus, MRI is diagnostic. Treated surgically by excision of the benign tumor ẃ is attached to the 8th cranial nerve.

Conductive & Nerve deafness differentiation

Weber test: tuning fork over middle of top of head, hearing is better on ear affected by conductive deafness because there is masking in the intact ear from combination of transmission of sound through air & bone conduction on intact ear.

Rinne`s test: tuning fork over the mastoid process, no perception of sound on the ear affected by nerve deafness. Audiogram is confirmatory.

Management

- Augmentin syrup 156, 312, 457mg, tab 612 mg, 50mg/Kg ÷3 X 5 days.
- Otal ear drops.
- Paracetamol drops 100, syrup 250, suppository 120, maximum daily dose = 1200 mg/day.
- Marcofen pedi. syp or suppository 100 mg, 1 X 2 for baby > 6 month age.
- Secretory otitis media may require myringotomy (ē no improvement), ventilation tube (grommet) ẃ extruded by itself.

Complications

- Chronic otitis media.
- Purulent otitis media.
- Perforation.
- Masoiditis.
- Brain abscess.

HUMAN IMMUNE DEFICIENCY VIRUS

Chronic infectious disease caused by HIV, characterized by spectrum starting from 1ry infection é or éout acute syndrome, followed by relatively long period of asymptomatic stage after ẃ in most pts progress to advanced &life threatening disease. The dis-ease was 1st recognized in 1981, in USA among homosexual males. HIV was clearly demonstrated in 1984 to be a causative agent for AIDS.

Epidemiology

The number of people living é HIV rose from around 8 million in 1990 to 34 million by the end of 2011, out of ẃ 2.3 million were children & 17.7 million were women. According to WHO, an estimated 2.1 million individuals worldwide became newly infected é HIV in 2013. Sub-Saharan Africa is the worst affected region é 25.7 million living é HIV, out of ẃ 2.1 million are children ˂15 yrs. The overall adult prevalence in this region is 5.9% & about 2.1 million deaths yearly. The incidence in many African countries varies from 5-30% of population. The IP is 1-3 yrs

Aetiology

HIV is retrovirus belongs to the subfamily of lente virus. There are 2 main types of the virus & many subtypes including:-

HIV-type 1: is the most common cause of HIV disease throughout the world & it has several groups & subtypes include the following:-

M group ẃ comprises 9 subtypes (A, B, C, D, F, G, H, J, K) as well as growing number of major circulating recombinant forms (e.g. AE, AG).

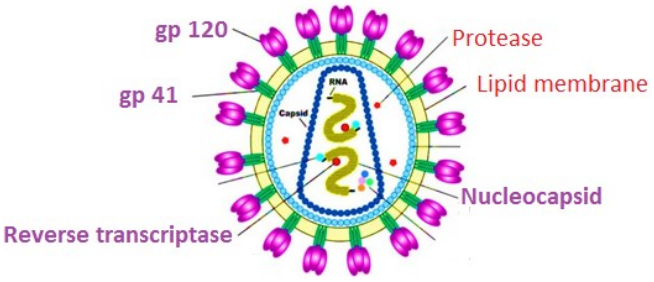
O group is relatively rare seen in Cameron & Gambia.

N group reported only in Cameron. In Africa: >75% of strains recovered to date have been subtypes A, C & DC. In Europe & Americas the subtype B is the predo-

minant strain. In Asia the recombinant forms such AE account of infections in South East Asia while subtype C is prevalent in India.

HIV-type 2 mostly confined to West Africa.

Morphology & characters



HIV is spherical shaped, the viral envelop is the most important part of the virus, has many small spikes consists of 2 important glycoproteins (gp), the gp 41 & gp 120, play an important role when the virus attaches to its host cells. The other important part of the virus is the viral capsid (core) ẃ contains 2 single stranded viral RNA & an important enzyme for the virus called reverse transcriptase enzyme ẃ plays important step in the life cycle of the virus, it converts the single stranded viral RNA into double stranded DNA (this process is called reverse transcription). HIV infect cells that express CD4 receptor molecules ẃ are present on various types of blood cells including lymphocytes, macrophages, monocytes, tissue cells (e.g. dendritic cells in genital tract & anorectic region) & glial cells of brain.

Pathogenesis

CD4 +ve T-Lymphocytes (T helper cells) play central role in body defence mechanism against infection, they mainly coordinate the cell mediated immune system & also as-sist the antibody mediated immune system. HIV has special affinity to CD4 T-cells & infects them. HIV infection characterized by profound immunodeficiency from progressive decline of T-helper cells.

Mode of transmission of HIV

Sexual transmission

Is major mode of transmission worldwide (90%). The virus was found in high quantities in the sexual fluids (seminal & vaginal fluid) of people é HIV infection, within the infected monocytes & in cell-free state. Anal sex appears to be the sexual practice carrying the highest risk of transmitting HIV. The reasons being rectal mucosa is thin, fragile & there are susceptible cells (Langerhans cells) in rectal mucosa. Vaginal sex also carry effective risk for transmission. The presence of other STDs as syphilis, gonorrhea ⇧ the risk of acquiring or transmitting HIV infection by several fold, as the quantity of virus in seminal or vaginal fluid significantly ⇧ & the number of infected monocyte is high around the genital area in pts é STDs.

Transmission through blood & blood products

IV drug abusers who share needles & syringes have high risk. Blood or blood products transfusion from infected donors (risk of infection is 90-100%). Transmission through sharp instruments, needles. There may be a risk of transmission from one pt to another or from an infected pt to health care provider.

Mother to child transmission

The risk of mother to child transmission is 30-45%. HIV may be transmitted from infected mothers to fetus during pregnancy (10% before the 3rd TM & 70% in late pregnancy or during labor), or through breast feeding in 10-15% of cases.

Mother to child transmission is by far the largest source of HIV infection in children < 15 years.

Clinical picture

The clinical consequences of HIV infection encompass a spectrum ranging from acute syndrome associated é primary infection to a prolonged asymptomatic state to advanced disease. Pt may present é recurrent bacterial, fungal or viral infection, failure to thrive, delayed milestones & wasting. In particular the pt is very susceptible to pneumocystis carinii, CMV, toxoplasma, infectious mononucleosis, Kaposi's sarcoma, chronic diarrhea & STDs.

Primary HIV Infection

Some pts are asymptomatic but 50% of infected individuals experience an acute clinical syndrome 3-6 wks after the primary infection. A flue like syndrome in ẃ symptoms persist from one to several wks & gradually subside. The typical presentation includes: •Fever. •Pharyngitis. •Lymphadenopathy. •Headache. •Arthralgia. •Myalgia. •Malaise. •GIT symptoms; anorexia, nausea, vomiting, diarrhoea. •Erythematous maculopapular rash & mucocutaneous ulceration. •Neurological symptoms; aseptic meningoencephalitis, HIV in CSF & peripheral neuropathy. Most pts (90%) recover spontaneously & 10% manifest a fulminate course of immunologic & clinical deterioration.

Asymptomatic stage-clinical latency

In most (90%) of pts, 1^{ry} infection é or éout the acute syndrome is followed by prolonged period of clinical latency. The length of time from initial infection to the development of clinical disease varies greatly (median is 7-10 yrs). Viral replication continues during this period. So there is no virologic latency. Rate of disease progression is directly correlated é HIV RNA levels. Pt é high levels of HIV RNA progress to symptomatic disease faster than do pt é low levels of HIV RNA.

The CD4 cell count fall progressively during this stage at an average rate of 50 cells/µl/year.

Early symptomatic diseases: pt begin to develop signs & symptoms when CD4 cell count is ‹500/µl. The clinical findings include:-

①Generalized lymphadenopathy: enlarged LNs (**>**1 cm) in 2 or more extra inguinal sites for **>**3 months éout obvious cause. Is often the earliest symptom of HIV infection after the 1ry infection.

②Oral lesions: usually indicative of fairly advanced immunologic decline, occurring in pt é CD4 count ‹300/µl. include:-

Oral thrush; ẃ appears as a white, cheesy exudates, often on an erythematous mucosa (most commonly seen on the soft palate) ẃ gives an erythematous or bleeding surface on scraping. When it involves the esophagus, pt complain of pain on swallowing. Is due to candidiasis.

Oral hairy leucoplakia: appears as filamentous white lesion, generally along the lateral borders of the tongue. Is presumed due to EBV.

Apthous ulcer: ulcer on oral cavity or pharynx of unknown etiology, usually are painful & may interfere é swallowing.

Herpes zoster (shingles): seen in 20% of pts. It is a reactivation syndrome of VZV. Indicates a modest decline in immune function &is often the 1st clinical indication of immunodeficiency. Lesions usually localized to a single dermatome & may extend over several dermatomes. A Frank cutaneous dissemination may be seen. It has a relapse rate of 20%.

③Thrombocytopenia: has immunologic base (due to autoimmune destruction of platelets). Very similar to ITP. Since most pts have platelet count ›50.000/µl, seri-

ous clinical problem are seen rarely. In some pts, when platelet count falls <10.000 clinical symptoms as bleeding of gums or extremity petechiae & easy bruisability are common presenting features. The bone marrow examination is normal or may show ⇧ in the megakaryocytes.

④Other clinical conditions: Molluscum contagiosum. Recurrent bouts of oral or genital herpes simplex & condylomata accuminata.

Staging of HIV/AIDS

There are different types of staging systems. The most common are:-

WHO Clinical Staging System for HIV/AIDS: designed for estimating the degree of immunosuppression on clinical criteria. Intended for use in pts. known to have HIV (i.e. HIV +ve antibody test). It is widely used in resource limited settings to make decisions as to when to start pt. on ART. According to this there are 4 clinical stages as shown in the following table:

stage 1	Asymptomatic
stage 2	Minor symptoms
stage 3	Moderate symptoms
stage 4	AIDS defining illnesses

Stage 1: •Asymptomatic. •PGL: defined as the presence of L.N. >1 cm size, in 2 extrainguinal sites & persisting for > 3 months.

Stage 2: •Unexplained moderate Wt loss (<10% of BW). •Recurrent URTI (sinusitis, tonsillitis, otitis media, pharyngitis). •Minor mucocutaneous manifestations (seborrheic dermatitis, fungal nail infections, recurrent oral ulcerations, angular chelitis).•Hepes zoster within the past 5 yrs (single dermatome).

Stage3: •Unexplained severe Wt loss (>10% of BW). •Unexplained chronic diarr-

hoea >1 month. •Unexplained prolonged fever >1 month. •Persistent oral candidiasis. •Oral hairy leucoplakia. •Pulmonary TB. •Severe bacterial infection (pneumonia, pyomyositis, meningitis, bacteremia), acute necrotizing ulcerative stomatitis, gingivitis or periodontitis. •Unexplained anemia (<8 gm/dl), neutropenia 500 /mm^3 &/or chronic thrombocytopenia (platelets <50,000/mm).

Stage 4: •HIV wasting syndrome. •Pneumocystis carinii pneumonia. •CNS toxoplasmosis. •Cryptosporidiosis or Isosporosis related watery diarrhea >1 month. •Extrapulmonary cryptococcosis. •CMV disease of organ other than liver, spleen, or LNs (e.g. retinitis). •Chronic herpes simplex infection as labial, genital or anorectal lasting for >1 month. •Disseminated mycosis (as histoplasmosis, coccidiodomycosis). •Oesophageal candidiasis (or involving trachea, or lungs). •Recurrent bacterial pneumonia. •Recurrent septicaemia. •Disseminated atypical mycobacterium. •Extrapulmonary TB. •Lymphoma (cerebral or B-cell non-Hodgkin). •Invasive cervical carcinoma. •Kaposi's sarcoma. •HIV encephalopathy. •HIV associated neuropathy.

The CDC staging system

Stage	CD4 count	CD4 %	Clinical Evidence
Stage 0	Early HIV infection		
Stage 1	> 500 cells/mm^3	> 26	No AIDS-defining condition
Stage 2	200-499 cells/mm^3	14-26	No AIDS-defining condition
Stage 3	< 200 cells/mm^3	< 14	or Documentation of AIDS-defining condition
Unknown	No data	No data	No information on presence of AIDS defining cond.

Comparison: WHO vs. CDC classification

•**WHO** classification does not require CD4 count & more appropriate to use in resource limited settings é high HIV prevalence.

•**CDC** clinical categories more dependent on expensive laboratories & is not adapted to resource poor settings.

Diagnosis of HIV

As mentioned before, the number of people living é HIV rose from around 8 million in 1990 to 34 million by the end of 2011, out of ẃ 2.3 million were children &17.7 million were women. So for all babies of infected mother you expect that all the babies will have antibodies (IgG) for HIV, this lasts for 12-18 months & 50% of those babies will have the disease. For diagnosis of neonatal AIDS we must isolate the virus, do PCR, qualitative & quantitative for viral load & to be repeated for confirmation.

① Serologic tests

a) HIV antibody tests: detect ABs formed by the immune system against HIV:-

ELISA used to be standard screening test for HIV, tests for number of ABs protein in combination. It is very sensitive test (99.5%) but not very specific. The test needs skilled personnel, takes several hrs & the +ve result needs to be confirmed by Western blot.

Western blot is excellent confirmatory test, has high specificity but relatively poor sensitivity, it should not be used for screening purpose.

Rapid HIV antibody tests have reasonably good sensitivity/specificity (>99%), easy logistically, does not need continuous water or electric supply in remote areas. Can be done by less skilled personnel & the interpretation of results is easy, the

test result can be made available in <30 minutes.

b) HIV antigen assays

Is P24 antigen capture assay, detects P-24 viral protein in the blood of HIV infected individuals. This viral protein can be detected during early infection, before seroconversion. This test is used to detect blood donors during the window period.

②DNA-PCR "Viral replication"

Extremely sensitive test, can detect 1-10 copies of HIV proviral DNA/ml of blood. It uses PCR technology to amplify proviral DNA. It is costly & needs sophisticated instruments & highly skilled professional. The chance of false +ve is high. Hence it should not be used for making initial diagnosis of HIV infection. It is often used to make early diagnosis of HIV in HIV exposed infants as serology tests are unable to diagnose HIV till the infant is 18 months old, or to diagnose or confirm virologic failure in pt who is not responding to ARTs.

③CD4 T cell count

Measuring CD4 cell count, is important indicator of the level of immune suppression that pt infected é HIV has. Average CD4 count of normal person is 1000-1200 /mm^3. Pt é HIV. The CD4 count drops by an average of 50-100 cells/yr. It tells you the level of immune damage. It should never be used to make diagnosis of HIV. The CD4 cell count may be variable depending on circumstances for example if there is diurnal variation (higher level at evening & lower at midnight), or é intercurrent infection, or é use of steroids, or in case of stress. In fact any of them can affect the CD4 count. Following the trend in CD4 count is useful in clinical decision making; for example; to decide eligibility of pt for ART,

or to follow the progress or failure of respond of the pt to ART.

④Additional tests

Should be done, include:- hepatitis markers, LFTs, kidney functions, FBS, ESR, CXR, AFB for TB, RPR for syphilis, blood film for malaria (in endemic areas), stool for parasites & pregnancy test for women in child bearing age.

Management

HIV infection progress to AIDS over 8-10 yrs, there Is no cure, but drugs help controlling the virus, enabling person to live healthy life.

Management of pregnant mother

If CD4 count <500, ARTs after the 14^{th} week of gestation, to be used &continued throughout pregnancy. Including; Zidovudine tab, 250mg 1X2 daily or Azidothymdine +ZDV, given IV 4 hrs before CS, amp 200mg in 20ml sol., dose is 2 mg/kg over 1 hr then 1 mg/kg/hr until umbilical cord clamped.

For resistant case: HAART should be used, it include; Efavirenz + Tenofaver+ Emtricitabine, accordin-g to certain protocol &follow up schedule for CD4 &PCR as will be discussed later

Management of Newborn

ZDV syrup 50 mg/tsp, 8 mg/Kg/day÷4 for 6 wks. If baby is preterm or unable to tolerate feed, IV infusion given, monitoring PCR/CD4 monthly for the first 4 months, then every 3-4 months up to the age of 1.5 year.

Septrin (40mg TMS + 200mg SMZ/5 ml), dose TMS 4-8mg /Kg ÷2, used as prophy-lactic for pneumocystis carini, from age 6 wks, continued for 6 months. Repeated blood & plasma transfusion ẃ must be irradiated to avoid graft versus host disea-se. No breast feeding &No BCG vaccine or other living vaccines for such baby.

Classes of Antiretroviral Therapies

①Nucleoside Reverse Transcriptase Inhibitors: structurally these drugs resemble naturally occurring nucleosides, break the formation of viral DNA by breaking the chain (chain breakers), they include;

Zidovudine (AZT) 300 mg PO BID, side effects; anemia, myalgia, bone marrow suppression.

Lamivudine (3TC) 150 mg BID or 300 QD, side effects; headache, occasional nausea. **Stavudine (d4T)** 40 mg BID for pt weight 〉60 kg &30 mg BID, for pt 〈60 kg, side effects; peripheral neuropathy ac-idosis & pancreatitis.

Abacavir (ABC) 1X300 mg tab. BID. Toxicity; hypersensitivity reaction occurs within the first 6 wks of initiation of Rx. Never rechallenge such pt. again é ABC.

Tenofevir (TDF) is actually, a nucleotide 1X300 mg tab, QD. Toxicity; headache, nausea, diarrhea, Lactic acidosis.

Didanosine (ddI) 1X400 mg enteric coated cap QD (if pt BW is > 60 kg, give 250 mg QD or 2X100 mg buffered tab BID. If pt BW is 〈60 kg, give 125 mg BID or 250mg QD. In case of using buffered tab, 2 or more tab must be used at each dose to provide adequate buffer, or 250 mg of reconstituted buffered powder BID. To be taken on empty stomach to avoid food interactions. Toxicity include; peripheral neuropathy, nausea, abdominal pain, pancreatitis & lactic acidosis.

②Non-Nucleoside Reverse Transcriptase Inhibitors: act by inhibiting the active site of reverse transcriptase enzyme. Include:-

Nevirapine (NVP, Nevipan®) 200 mg QD X2 wks, then 200 mg BID. Toxicity; skin rash (17%) ẃ may be in a milder form (dry rash) as erythematous or maculopa-pular, in such case continue Rx é close observation &antihistaminic may be given.

The skin rash may be severe (wet rash) é mm involvement, Steven's Johnson sy & toxic epidermal necrolysis, such case need discontinuation of the drug & never rechallenge. Hepatitis is another side effect.

Efavirenz (EFV, Stocrin®) 3X200 mg capsules or 600 mg/day PO to be taken é low -fat meal because high-fat ⇧ its absorption by 50% leading to ⇧ of its side effects. Toxicity of EFV include; CNS changes in 52% of cases; insomnia, night-mares, poor concentration, mood change, dizziness, disequilibrium, depression, psychosis. Skin rash in 15-27% of cases usually does not require discontinuation. This drug is contraindicated during pregnancy.

③Protease Inhibitors: act by inhibiting viral assembly. Include:-

- **Ritonavir (Norvir).**
- **Lopinavir + Ritonavir (Kaletra).**
- **Nelfinavir (Viracept).**
- **Saquinavir-HGC (Invirase).**

The side effects of this group include; glucose intolerance (DM in some pts), hypertriglyceridemia, lipodystrophy; morphologic changes, at accumulation in the lower part of the body é atrophy of facial fat.

Goals of HAART (Highly Active Antiretroviral Treatment)

①To improve the length & quality of the pt`s life.

②To ⇧ the total lymphocytic & CD4 cell counts, allowing preservation or impro-vement of the immune function.

③To Keep HIV RNA < 400 copies/ml within 4-6 months of ART initiation.

④To reduce HIV-related morbidity & mortality. HAART is not a cure for HIV. If Rx stopped, the virus will continue to replicate, it cannot eliminate HIV completely.

What does HAART require to be effective?

•Strict adherence to the Rx regimen & proper monitoring of side effects & disease progression. Recognition & Rx of comorbidities & recognition of drug interactions •Baseline assessment before initiation of HAART. •Baseline medical history. •Physical examination & clinical staging. •Laboratory testing….

All together lead to development of the pt care plan.

WHO criteria to initiate ART in adults & adolescents

Stage	CD4 testing not available	CD4 testing available
1	Don't treat	Start ART if CD4 count is < 200
2	ART may be started if the TLC is <1200	
3	If symptomatic initiate ART irrespective of TLC	Start ART if CD4 is <350
4	Start ART irrespective of TLC	Start ART irrespective of CD4 count

HIV/AIDS associated illnesses

Opportunistic infections (OIs) & Opportunistic malignancies (OMs): develop as a result of HIV-inflicted damage to the immune system & are leading causes of morbidity & mortality in HIV-infected persons. Most of the common OIs are preventable as well as treatable. In resource-limited settings, it may be difficult to diagnose & treat OIs.

The **OIs** develop when the CD4 count is <200 cells/ml & include:-

Bacterial: Streptococcal, Staph, H. Influenza & G -ve bacteria. Mycobacterial: M. TB, M. kansasi & M. Aveum.

Fungal: PCP, Cryptococcus Neofrmans, Histoplasmosis, Coccidiodeocomycosis.

Viral: CMV, HSV infection.

Parasitic: Toxoplasmosis & Strongyloidosis.

The **OMs** are neoplastic conditions, tend to occur more frequently in pt é underlying immunodeficiency, including; pulm. Kaposi's sarcoma or Non-Hodgkin lymphoma. The type of OIs or OMs that pt develops depend on the degree of immunosuppression i.e. each of the OIs & OMs typically develop at or below characteristic CD4 cell count range. So CD4 is an excellent indicator of the risk of developing specific OIs or OMs. Knowing the disease stage will be useful in limiting the different- ial diagnosis. In advanced stages, a person may be infected by > one pathogen.

Opportunistic infections

Respiratory system

Is the most common site of HIV-associated complications/illnesses & are the leading cause of morbidity & mortality. Many of the respiratory problems are both preventable & treatable. Therefore, prevention, evaluation & treatment of pulmonary disease is essential part of managing AIDS. There is wide spectrum of pulmonary manifestations including the following:-Respiratory manifestations at any level of CD4 count: URTI: sinusitis, pharyngitis, acute bronchitis, bacterial pneumonia, TB & non-Hodgkin's lymphoma. Respiratory manifestations at CD4 count $<500/mm^3$ include; bacterial pneumonia. pulmonary TB. Respiratory manifestaions at CD4 count $<200/mm^3$ include: pneumocystis carinii or cryptococcus neoformans pneumonias. Respiratory manifestations at CD4 count $<100/mm^3$ include: pulmonary Kaposi's sarcoma, bacterial pneumonia (G-ve bacilli & staph aureus) &Toxoplasma pneum. Respiratory manifestations at CD4 count $<50/mm^3$ include: disseminated histoplasma capsulatum or coccidioides immitis, CMV pneumonitis, disseminated mycobacterium avium complex, disseminated mycobact-

erium (non-TB) & aspergillus species pneumonia.

Bacterial pneumonia

Common agents: streptococcal pneumonia, as the degree of immunosuppression worsens, pneumonia may be recurrent & associated é sepsis.

Clinical presentation

Abrupt onset é fever, cough, production of purulent sputum, dyspnoea &pleuritic chest pain.

Investigations: CXR, CBC, blood culture, gram stain & sputum culture. The common findings in X ray are; pneumonic consolidation, infiltrates, or pleural effusion.

Treatment

Antibiotics: Penicillin (Procaine or Crystalline), Amoxicillin or Fluoroquinolones.

Pneumocystis carinii pneumonia

Etiologic agent: P. jiroveci is fungus.

Epidemiology: one of the commonest OIs, however the incidence has declined over the yrs due to HAART & use of CPT. 50% of pts experience at least 1 bout of PCP during their Lifetime. Infection transmitted from human or environment.

Clinical presentation: indolent course characterized by wks of vague symptoms prior to presentation or diagnosis. The median duration of symptom is 28 days. Dyspnoea & fever are the cardinal symptom. Cough é scanty sputum seen in >2/3 of cases. The physical findings are minimal, the usual findings for pneumonia may not be noted; RD ±cyanosis, little abnormality on chest examination, rhonchi may be heard, especially in pt é some other underlying pulm disease, findings of consolidation are usually absent. P carini appears to be capable of haematogenous spread & seeding a variety of organ systems as well as causing ear infection.

Diagnostic work-up

CXR: could be normal or shows diffuse bilateral alveolar/interstitial infiltrates is the usual findings.

LDH: ⇧ in >90% of cases & has a very high -ve predictive value i.e. if LDH level is low in a pt, the diagnosis of PCP is less likely.

Definitive diagnosis

By demonstration of Trophozoites/cyst from the organisms in samples obtained from induced sputum in ẃ the yield is 60% or bronchoalveolar lavage in ẃ the yield is 95%. Staining; wright- Giemsa, Methenamine silver, Direct IF, nPCR. Other tests: Gallium 67 scan, PFT, & ABG.

Treatment

Antibiotics: the gold standard for Rx is Cotrimoxazole IV or PO. It is effective in **>** 90% of pts, dose 15 mg/kg/day (Trimethoprim) in 3-4 divided doses, for 21 days. The major disadvantage is the relatively high incidence of side effects; rash, fever, leucopenia 10% (HIV-ve) Vs 50% (HIV +ve). The response to Rx may not occur unt-il the end of 1st wk & the pt may get worse during the first few days owing to the inflammatory response resulting from the death of large number of organisms in the lungs. Alternative regimens is Clindamycin 600 mg IV q 8 hrs, or 300-400 mg PO q 6 hrs + Primaquine 15-30 mg base/day X 21 days, or Pentamidine 4 mg/kg/day IV X 21 days, or Atovaquone 750 mg PO bid é meal X 21 days.

Adjuvant Rx: O_2 supplementation may needed, the use of steroids ⇩ mortality by 50 % & ⇩ the need for mechanical ventilation & is indicated if pt is; moderately distressed or cyanotic or PaO_2 **<**70 mmHg. Prednisone 40 mg PO bid for 5 days or 20 mg/day for 11 days followed by gradual weaning.

Primary Prophylaxis: strongly recommended for HIV infected person é evidence of significant immune deficiency: CD4 count **<**200/µl (CD4 cell % of **<** 15% in children) or é associated thrush or PUO.

Secondary prophylaxis: indicated for pt é prior episode of PCP. TMP-SMX 2 tab /day (single strength), or TMP-SMX 2 tab 3 times/wk. An alternative regimens is Dapsone 100mg PO daily, or Dapsone 50mg PO daily + Pyrimethamine 50mg PO weekly + Leucovirin 25 mg PO weekly. Aerosolized Pentamidine 300mg/month via nebulizer. Atovaqoune 1500mg daily. N.B. the prevention of PCP may also be beneficial in ⇩ the risk of having other HIV associated infections such as CNS toxoplasmosis & other bacterial infections.

Tuberculosis

Is the leading OIs in developing countries. There ⇧ incidence & prevalence of TB in HIV infected pt. The lifetime risk of developing TB is 50% among HIV +ve compared to 5-10% in HIV-ve pts. HIV is the most potent factor known to ⇧ the risk of progression from M. TB infection to active disease. The seroprevalence of HIV among TB pts range from 30-60%. The next table differentiate the early & late manifestations of TB, according to the CD4 count.

Challenges/Problems

⇧Morbidity, mortality & high case fatality rate. ⇧ Drug toxicity & interaction between anti-TB drugs & ARTs. Also the ⇩ of drug absorption &high pill burden may ⇩ adherence to Rx.

Impact of TB on HIV: TB hastens the rate of HIV progression & it is the leading cause of illness & death among HIV/AIDS pts.

Tuberculosis	Early stage, CD4 >200	Late stage, CD4 count < 200/mm^3
Clinical Picture	Similar to non HIV infectedé productive cough. Pulm. manifestations are dominate	Atypical presentation: extrapulm. TB more common. TB tends to disseminate (involving different organs like meninges, pleura, LNs)
Sputum Smear PPD	Often +ve Reactive é >10 mm.	Often -ve Often -ve or anergetic.
CXR	Typical findings of TB upper lobe & or bilateral infiltrates. Cavitations. Pulm. fibrosis	Atypical: interstitial infiltrates especially in lower zones é no features of cavitation/fibr- osis. A -ve CXR may associated é sputum+ve AFB (12%). In the setting of HIV epidemic, it is no longer possible to look at CXR & say that it is TB or not TB!

Treatment

When TB & HIV are coexisting, TB is more life threatening & should be treated first & pt should be stabilized. The same combination anti-TB drugs are given based on the Rx category. Close follow up of pt on DOTS is required. Complete cure from TB may be achieved in 6-8 months. Most pts who have TB-HIV coinfection are eligible for ART. When to start ART in pt on anti-TB drugs depends on CD4 & the clinical condition. If CD4 $<50/mm^3$, start ART as soon as the pt tolerates the anti-TB drugs. If CD4 count 50-200 mm^3, start ART after completion of intensive phase of DOTs. If CD4 >200 mm^3, ART can initiated after compilation of anti-TB treatment.

INH preventive therapy

Rationale: life time risk of having active TB in pt é HIV is 50% é annual risk of 7-9% (compared to only 5-10% life time risk in non HIV infected). It is advisable to give INH prophylaxis & the pt should screened for active TB before giving preventive Rx INH 300 mg/day for 6-9 months. Alternatively, Rifampicin for 4 months.

Neurological manifestations

The nervous system is the 2nd commonly affected system next to respiratory system in HIV infected person & is common cause of morbidity & mortality. Seen in 7-20% of pts é initial AIDS diagnosis & > 90% in post mortem studies. Neurological manifestations occur at any stage of HIV infection. All levels of neuroaxis can be involved & the clinical manifestations are variable.

Pathogenetic mechanisms

- *Directly related to HIV:* include; Aseptic meningitis, Dementia complex, Myelopathy, Peripheral Neuropathy (acute demyelinating distal polyneuropathy), Mononuritis Multiplex, Distal Sensory Polyneuropathy, Myopathy, or Vasculitis.
- Secondary to Immunodeficiency: including; CNS Toxoplasmosis, Cryptococcal or TB Meningitis/Tuberculoma, Progressive Multifocal Leukoencephalopathy, Neurosyphilis, CMV or Polyradiculopathy/Encephaliis. Primary CNS Lymphoma.
- Related to ARTs: drugs causing peripheral neuropathy as d4T & DDI. Drugs causing myopathy as ē ZDV, or causing psychiatric manifestations as é EFV.

Aseptic meningitis

May occur at any time in the course of HIV infection, most commonly at time of acute HIV infection. However it becomes increasingly rare. Pts experience head ache, photophobia, sometimes frank encephalitis & cranial nerve involvement

(commonly the VII nerve). Diagnosis: the CSF will show lymphocyte pleocytosis 10-100 cells/µl + ⇧ protein & normal BG level. The symptoms usually resolves within 2-4 wks. The HIV serology may be negative if it occurs during the 1ry HIV infection. To confirm diagnosis of HIV, p24 antigen or DNA PCR may be done or repeat HIV serology after few weeks.

CNS Toxoplasmosis

Toxoplasmosis is caused by protozoa "Toxoplasma Gondi". It is a zoonotic infection, cats are definite hosts & excrete the oocysts in their faeces & can be transmitted from animals to humans. Toxoplasma Gondi cysts also found in undercooked meat .Is the most common cause of secondary CNS infection in pt. é AIDS. It is generally late complication of HIV infection, usually occurs when CD4 cell count <100/ mm^3. It is thought to represent a reactivation of prior infection.

Clinical features: onset is subacute é fever, headache, hemiparesis, seizures & altered mentation. Over 90% of pts present é focal neurologic deficits & 10% of pts present é encephalitis picture; confusion or coma & become more toxic. The commonly affected areas are the basal ganglia, brain stem & cerebellum. The extracranial manifestation of toxoplasmosis include; retinitis, myocarditis & pneumonitis

Diagnosis: CT/MRI; multiple ring enhancing lesions are the findings in 90% of cases é mass effect & oedema. Preferential location are basal ganglia, grey-white junction & white matter. The serologic assays are of limited value. A -ve toxoplasma AB test makes the diagnosis less likely.

Treatment

Regimen 1: loading dose of Pyrimethamine 50-75mg/day for 2-3 days followed

by 50mg/day +Sulfadiazine 2-4 gm/D in divided doses, PO + Folinic acid 10 mg/D.

Regimen2

Pyrimethamine & Leucovorin **+** Clindamycin 450 mg q8 hrs for 6 wks, or 3 wks after complete resolution of lesions on CT scan. Continue suppressive Rx for life (Pyrimethamine 25mg/day **+** Sulfadiazine 2 gm/day & Folinic acid 10 mg/ day). This regimen is associated é high rate of adverse reactions.

Regimen3

Fansidar (is combination of Pyrimethamine 25 mg + Sulfadoxin 500 mg) 2 tab PO BID for 2 days, then 1 tab/day + Folinic acid. If pt is very critical, add Doxycycline 100 mg PO BID. Side effects of Fansidar include; leukopenia is the main side effect. Higher dose of Fansidar (2 tab/D) has been found to be associated é frequent incidence of fatal Hge. Check for bleeding tendency; gum bleeding, epistaxis, hematuria. Do Hb, WBC & platelet count once/wk, to prevent these side effects & give Folinic 10 mg PO/day or advice to take cream cake daily. If there is bleeding tendency, stop Fansidar & start Doxycycline 100 mg PO BID. Alternatives: Cotrimoxazole or Clindamycin + Pyrimethamine/Azithromycin, Clarithromycin.

Indications for steroids: evidence of marked ⇧ of ICP & altered mentation.

Dexamethasone 8 mg IV stat, then 4 mg IV QID, for 2 days.

Suppressive Rx: Fansidar 1 tab/day should be continued. Can be stopped when the CD4 count is > 200 for 6 months.

Preventive Rx: indicated if CD4 cell count ˂100 cells. TMP-SMX 2 tab/day or 2 tab 3 times/wk. Alternative regimens: Dapsone + Pyrimethamine + Leucovorin. The preventive Rx can be stopped if CD4 count ˃200 cells/ml for ˃3 months following HAART.

Cryptococcal Meningitis

Aetiology: is yeast-like fungus. Pigeon droppings commonly contains serotypes A or D. The infection acquired through inhalation.

Epidemiology

Is the leading cause of meningitis in pt é AIDS & is the initial AIDS defining illness in 2% of pts. Particularly common in pts é AIDS in Africa.

Clinical features

Occurs late in the course of the disease when CD4 <100/mm^3. CNS & meningeal involvement seen in 67-85% of pts. Papilledema seen in 30 % of pts. Neck stiffeness, photophobia, meningeal signs seen in 30% of pts. Low grade fever, nausea, vomiting & headache. Both fever & nuchal rigidity are often mild or lacking. The late manifestations include; confusion, altered consciousness, coma, extracranial manifestations: include pulmonary disease, disseminated disease(10 % of cases), fungemia, lymphadenopathy, cutaneous cryptococcosis (centrally umblicated multiple lesions on the face (looks like molluscum contagiosum).

Diagnosis

- CSF analysis: opening pressure of CSF is high. The WBC differential, protein & glucose are normal in 1/3 of pts. The Indian ink is +ve in 60-80% CSF.
- Cryptococcal Ag is +ve in 95-99 %.
- Cryptococcal culture is gold standard.

Treatment

Induction; Amphotericin B (é or é/out Flucytosine) 0.7mg/kg for 2-3 wks, followed by consolidation: Fluconazole 400mg, PO, daily for 8-10 wks or until CSF is sterile. Maintenance Rx using Fluconazole, 200mg, PO, daily life long.

If CSF opening pressure raised, do drainage until CSF pressure is < 200mmH_2O & repeat LP daily until stable or CSF pressure normalizes. There is no place for Dexamethasone & discontinue the maintenance prophylaxis when the CD4 count >200/mm3 for >6 months.

Progressive Multifocal Leukoencephalopathy

Epidemiology: reactivation of JC virus seen in 2-4% of AIDS pts.

Clinical presentation

Occurs late in the course of HIV when CD4 count is <100. Subacute onset, pt is afebrile, alert, no headache, multifocal neurologic deficit. Classic triad include;

Dementia, Hemiparesis & Hemianopia.

Diagnosis

- CSF often non-diagnostic.
- JCV PCR may help to make diagnosis.
- Serology: 90% adults are sero positive for JC virus.

Treatment: no effective Rx, but initiation of HAART ⇧ survival.

Primary CNS Lymphoma

Clinical presentation

- Occurs late in the course of HIV when CD4 count is <100. Seen in 4% of AID pts.
- Confusion, lethargy, memory loss- seen in 57% of cases.
- Hemiparesis or Aphasia- seen in 40% of cases.
- Seizures- seen in 14% of cases.
- Cranial nerve palsy- seen in 9% of cases.
- Headaches- seen in 3% of cases. No fever unless concomitant infection.

Diagnosis

•CT/MRI: multiple lesions as frequent as single lesion, irregular & solid enhancement, subependymal enhancement are more specific, variable mass effect. Localization mainly periventricular.

•CSF: EBV DNA PCR (sensitivity 85% & specificity 98%).

•Histology: diffusely infiltrating, multicentric tumor of B cell lineage é the presence of EBV genome in ~100%.

Treatment

- Cytotoxic drugs is not effective. Radiotherapy can help some pts.

- Response to steroids is variable.

Dementia Complex

Is the first AIDS defining illness in up to 5-10% of pts é AIDS & is the major cause of dementia in young people. Its major feature is the development of dementia (decline in cognitive ability from a previous level). Characterized by triad of:-

•Cognitive. •Behavioural. & •Motor dysfunction.

Stages of ADIS Dementia Complex

	Cognition	Behaviour	Motor
Early	Inability to concentrate	Altered personality	
Mid	Mental slowing, Forgetfulness	Social withdrawal	Poor coordinate
Late	Global dementia	Apathy	Paraparesis

Diagnosis

Neuropsychological tests. Mini-mental test. Is often a diagnosis of exclusion.

Treatment

Most pts improve é HAART é possible benefit from ART that penetrate CNS.

Peripheral Neuropathies

Occurs in 30% of pts é AIDS. Include:-

- Mononeuropathy e.g. Bell's palsy.
- Mononuritis multiplex.
- Distal sensory peripheral polyneuropathy (the most common).

The peripheral neuropathies may be caused by HIV infection or ART mainly the d4T & DDI drugs. Presents é symmetric bilateral painful burning sensation, para-esthesia, tingling of the feet & LL.

Diagnosis

- Nerve conduction study.
- Exclusion of other causes.

Treatment

Symptomatic & discontinuation or changing the drug ẃ is causing it.

Seizure

Relatively frequent complication of HIV infection. May be a consequence of OIs or OMs. The seizure threshold is often < normal in pt é HIV infection owing to the frequent presence of electrolyte abnormalities & it may be the presenting clinical symptom of HIV disease.

Causes

CNS toxoplasmosis 25% of pts. Primary CNS lymphoma 20% of pts. Cryptococcal meningitis 8% of pts. HIV encephalopathy 7-50%.

Treatment: Anticonvulsant indicated to all pts é HIV inf. associated é seizures, unless a rapidly correctable cause is found. Phenytoin (100mg PO TID) remains the Rx of choice, Phenobarb (100mg PO daily) or Valproic acid are alternatives.

GIT manifestations

Candidiasis: caused by Candida Albicans, include the following:-

Oral Candidiasis

Appears as white, cheesy exudates, often on an erythematous mucosa (most commonly on soft palate) ẃ gives an erythematous or bleeding surface on scraping.

Treatment: Nystatin suspension 2.5-5 ml gargled 5 X daily. 2% Miconazole oral gel applied 2-3 X daily. Amphotericin B lozenges. Fluconazole 100-200 mg PO/day for 7-14 days in severe cases. Oral hygiene, D/C steroids/antibiotics if pt is taking.

Oesophageal Candidiasis

Usually coincides é CD4 count of ˂50. Causes substantial pain or sense of obstruction on swallowing. Most lesions occur on distal 1/3 of the oesophagus & appear on endoscopy as redness, oedema & focal white patches or ulcers. If HIV infected person has oral thrush & substernal pain on swallowing presumed diagnosis of oesophageal candidiasis can be made. Endoscopy would prove the diagnosis, but is unnecessary if the pt responds to antifungal treatment. A linear ulcerations of oesophagus may be seen on barium X ray.

Treatment

The 1st line is Fluconazole 200 mg/day PO (maximum 400 mg/day) for 14-21 days.

Diarrhea

Common clinical condition in HIV infected pts (**>** 50% of cases). May be acute or chronic, watery, mucoid or bloody. May be associated é fever. Pathogens may be bacterial, viral, protozoal, fungal, spirochaetal, mycobacterial, or others (malignancies). The mechanism of diarrhoea is through adhesion to mucosal surface, enterotoxin enteroinvasion & atrophy of mucosal surface.

Chronic diarrhea

Diarrhea lasting for >2 wks é a single watery bowel motion &/or 3 or more loose stools/day. Diarrhea occurs in 60% of HIV +ve cases. Frequency of diarrhea ⇧ as the CD4 count falls. The incidence of chronic diarrhea ⇩ é HAART. The protozoa causing ch. diarrhea in HIV pts include; Cryptosporidium & Microsporidium.

Enteropathy

Chronic diarrhea for ẃ no etiologic agent other than HIV can be identified. It is most likely a direct result of HIV infection.

Clinical features: in the early stage it is intermittent self-limiting diarrhea, however in advanced stage it may be persistent life threatening diarrhea presenting é copious amount of stool several times/day associated é abdominal cramp, nausea & vomiting may be also present. Significant weight loss (wasting) may occur due to the associated malabsorption. Fluid & electrolyte depletion.

Investigation

- Stool microscopy & culture.
- Intestinal biopsy.
- Special stains: modified AFB stain.

Treatment

1. General Rx of chronic diarrhea include: Hydration: oral or parenteral é electrolyte replacement. Symptomatic treatment include; antidiarrheal agents (Loperamide 2-4 mg QID- Lomotil 5 mg QID).
2. Specific Rx: for Cryptosporidium: Paromomycin 1 gm BID + Azithromycin 600 mg QD For Isospora: Cotrimoxazole 2 tab QID for 10 days, then bid for 3 wks, or Pyrimethamine 75 mg + Folinic acid. For secondary prevention we use Cotrimoxa-

zole 2 tab/day or Pyrimethamine 25 mg + Folinic acid 5 mg QD.

Problem: malabsorption of drugs.

Strongyloidosis

Parasitic infection caused by strongyliod stercolaris. Acquired thr-ough skin penetration of its larva form. Usually mild disease in immunocompetent individuals, but disseminated infection common in immunocompromised hosts & systemic manifestation may mimic sepsis.

Manifestation: asymptomatic or mild symptoms in immunocompetent individuals é occasional severe pruritus. May manifest é mild diarrhea & epigastric pain. In immunocompromised pt a large amount of filariform larva are released & may invade the GIT causing enteritis é severe diarrhea & malabsorption, or the filariform larva invade the lungs causing cough, shortness of breath (Loffler pneumonia). The CNS, peritoneum or liver may invaded. Severe systemic symptoms are commonly seen in disseminated infection & may be complicated by G -ve sepsis.

Treatment: Ivermectine 200 µg 1-2 days, or Thiabendazole 75 mg/kg bid for 3 days. Or Albendazole 400 mg/day for 5 days.

Skin Manifestations

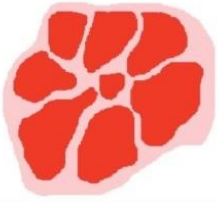
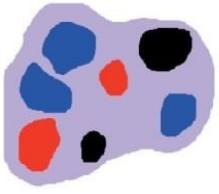
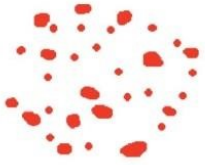
80-90% of HIV pts have skin manifestation. Skin problems could be the first organ system affected. Various type of skin disease occur.

Classification

•Infections: bacterial. staph aureus is common pathogen. The common manifestations of it are:- Bullous impetigo, Folliculitits, Furuncle, Carbuncle & Cellulitis.

•Infestations; parasites. •Inflammatory conditions.•Malignancy.

Treatment: topical or systemic antibiotics depending on the severity.

					
Lesion	**Angioma**	**Pyogenic Granuloma**	**Angiokeratoma**	**Angioma Serpiginosum**	**Kaposi Sarcoma**
Type of vessels	Red lacunae	Wide variety: dotted, hairpin, linear irregular, and polymorphous	Dark lacunae and red lacunae	Small red lacunae	Rainbow pattern (areas with different colors in the same lesion)
Distribution	Regular and well-demarcated	Nonspecific	Nonspecific	Regular, scattered throughout the lesion	Nonspecific
Additional criteria	- Absence of blood vessels or other structures inside	- Homogeneous reddish area - Peripheral whitish collarette - White lines that cross the lesion	- Whitish veil - Erythema - Hemorrhagic crusts	- Absence of other dermatoscopically visible structures	- Homogeneous bluish-red pigmentation - Lacunae - Scaling surface
Diagram					

Syphilis

Has atypical presentations in HIV pts, the 1ry chancre is usually painless, can be tender. The latent period before development of meningovascular syphilis is shorter & rapidly progresses to tertiary syphilis. Relapses éout reexposure.

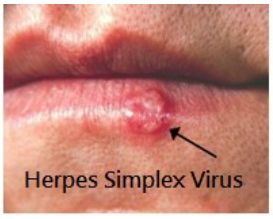
Investigations

- Screening tests (VDRL/RPR).
- Specific test (FT-AB absorption T).

Treatment

Benzathin Penicillin 2.4 mega unit IM weekly for 3 doses. Penicillin IV/ 2-4 mega unit every 4 hrs for 10-14 days, in case of CNS involvement. Follow up at intervals of 1, 2, 3, 6, 9 & 12 months.

Herpes Simplex Virus



Is due to reactivation of latent virus. The usual manifestations are grouped vesicle é erythematous base. In HIV infected pts however may presented é atypical presentation as chronic non healing deep ulcer, verrucous erosion, or mixed infection are common. High frequency of reactivation. Widespread local extension. Higher incidence of dissemination, viremic spread to visceral organs, ẃ is life threatening.

Treatment

Systemic Acyclovir tab 200 mg, amp 250 mg, 15 mg/kg/day ÷3 for 5-10 days. Acyclovir 50 mg/kg/8 hrs where absorption is poor. Acyclovir 400 mg 2 X day in frequuent relapse. Famcyclovir 125 mg 2X daily for 5 days.

Herpes Zoster Virus

Varicella Zoster Virus

There is ⇧ incidence of HZV infection in pt é HIV infection & it is one of the earliest OIs to occur.

Clinical picture: are atypical presentation, may present é hemorrhagic necrotic or chronic verrucous lesions or multiple dermatomal involvement. Tendency to be generalized. May occur recurrently.

Treatment: Primary varicella: Acyclovir IV 10 mg/kg/8 hrs for 7-10 days. Herpes

zoster: Acyclovir 800 mg 5 X a day for 7-10 days.

Human Papilloma Virus

Human Papilloma Virus

Wart is common infection in HIV. Refractory to Rx & its complications include; neoplastic changes & ⇧ risk of cervical carcinoma.

Treatment: Podophyllin 20% or 5-Fluorouracil. or Cryotherapy or excision if big.

Molluscum Contagiosum

Molluscum Contagiosum

Caused by pox virus. Occurs in HIV pt é low CD4 count. Atypical presentations are common. Commonly seen in children. Tends to be generalized, giant molluscum contagiosum & secondary infection.

Treatment: cryosurgery or Curettage or Electrosurgery. Podophyllin or Canta-ridine or 5-Fluorouracil.

Pruritic Papular Eruption

Chronic itchy condition commonly seen in HIV infected pts. Prevalence 46% in HIV infected persons. Symmetrical non-follicular papules in the trunk & extensors of extremities.

Diagnosis: biopsy.

Treatment: Topical antipruritic lotion, Corticosteroid, Oatmeal bath, Systemic antihistaminic. or Phototherapy, UV-B,UVA+ Psoralen.

Cytomegalovirus

High incidence, 30-40% of the general population are +ve for AB of CMV & >90% of IV drug abusers are +ve. 20-30% of pts. é AIDS had CMV reactivation prior to the era of HAART.

Clinical Picture

*CMV retinitis: visual disturbances, floaters, flashes of light, photophobia, blurring of vision, painless &gradual loss of vision, usually bilateral. Diagnosis confirmed by retinal examination.

*CMV esophageal ulcers: pain& difficulty in swallowing. Diagnosis by T. biopsy.

*CMV colitis: abdominal pain, watery diarrhea, sometimes bloody, rarely perforation, fever. Diagnosis by tissue biopsy.

Treatment

Valganciclovir (PO). Ganciclovir (IV). Ganciclovir Intraocular implant.

Visceral Leishmaniasis

Ccaused by *L. Donovanii* (protozoa). Has become an important OIs among perso ns infected é HIV-1. Most coinfected pts have CD4 cell count <200. The infections affect the same cell lines, causing cumulative deficiency of the immuneresponse. Pts present é fever, organomegaly, anemia/pancytopenia. Presentation could be atypical, but VL should be suspected in those é travel history to endemic areas.

Diagnosis

- Serological tests are less sensitive in immunocompromised pt.
- Parasite could be detected in peripheral blood in immunocomprmised pts.
- Bone marrow aspirate.
- Splenic aspirate (most sensitive).

Treatment

First line: Pentavalent antimonials. Alternatives: Pentamidine, Amphotericin B.

The relapse & toxicity are common in pts coinfected é HIV.

Opportunistic Malignancies

Kaposi's sarcoma

Etiology/Pathogenesis

Multifactorial. Vascular neoplasm affecting the skin & mucosa. Immunosuppression ⇧ the risk of KS 500 times >general population. Presence of HHV-8 found in all types of KS. The HIV Tat protein potentiates the milieu conducive to KS growth

Transmission

Studies have shown that HHV-8 ẃ is the etiologic agent for KS is believed to be sexually transmitted. The risk factors are multiple partners, history of STDs & being HIV +ve. More common in homosexual men. Multiple heterosexual contacts is a risk factor for HHV-8 in Africa. IV drug users, or via saliva as the HHV-8 titre 2-3 times higher in saliva than in semen, anorectal or prostate fluid samples.

Epidemiology

KS is the most common OMs among HIV +ve pts. The incidence of KS has declined by 66% é the use of HAART.

Clinical Picture

Can affect almost any organ system. Most common sites include:-

Skin: flat/nodular lesions; can progress to significant infiltration of skin & necrosis. Oral cavity: flat to invasive lesions.

GIT: can have KS anywhere in GIT, ẃ can cause intestinal blockage & bleeding.

Pulmonary: can spread along bronchi & vessels.

Diagnosis

Skin & oral lesions can be diagnosed by visual examination even though skin biopsy is most accurate to make diagnosis. Resolution of skin lesions é HAART can give presumptive diagnosis. Testing for HV-8 is more research than clinically applicable. Lung & GIT lesion would need endoscopy & biopsy.

Treatment

Primary Rx: lesions significantly regress é HAART. Local Rx for skin lesions:-

- Alitretinoin gel (35-50% response).
- Local radiation (20-70% response).
- Intralesional Vinblastine/Vincristine (70-90% response).
- Cryotherapy (85% response).
- Photodynamic Rx or surgical.

Systemic Rx: immunotherapy; Interferon-α: immunomodulatory antiviral & antiangiogenic. This Rx may have superior efficacy if combined é HAART. Indicated for rapidly progresssive oral or visceral disease. Liposomal Doxorubicin/ Daunorubicin is superior to conventional chemotherapy é less toxicity.

Lymphomas

There are 120 X ⇧ incidence of lymphoma among HIV pts. 6% of all AIDS pts develop lymphoma at some time in the course of their illness. As HIV disease progress the risk of lymphoma ⇧. The incidence of lymphoma hasn't shown dramatic ⇩ even after HAART is being widely used by HIV pts worldwide. Lymphoma is a late manifestation & often occurs when CD4 count is <200.

Categories

❍ Grade III or IV immunoblastic lymphoma (60%).

❍Burkett's (20%) associated to EBV. ❍ Primary CNS lymphoma.

Treatment

✶In pt é high CD4 count -intensive chemotherapy

✶In pt é low CD4 count - a low dose chemotherapy.

✶Palliative measures to ⇩ the size of lesion & associated oedema: RT + steroid.

Cervical cancer

There is 5 fold risk of developing cervical cancer in women é AIDS. Is associated é human papilloma virus infection. Invasive cancer of the cervix is an AIDS defining illness. Abnormal PAP smear is seen in 60% of HIV infected women.

TUBERCULOSIS

Chronic necrotizing disease caused by mycobacterium TB complex. Usually affects the lungs but almost all organs may be affected. Classified into:-

Pulmonary TB accounts for 80 % of all TB cases. Smear +ve accounts 75-80% of all pulmonary TB cases while smear -ve accounts 20-25%.

Extrapulmonary TB accounts for 20% of all TB cases.

Aetiology

Mycobacterium belongs to the mycobacteriaceae family. The species commonly involved are M. Tuberculosis, M. Bovis, M. Africanum & M. Microti. But of all, M. Tuberculosis is by far the commonest. M. tuberculosis is a rod-shaped, non-spore forming, thin aerobic bacterium measuring about 0.5 X 3µm. The bacterium is demonstrated by acid fast staining technique.

Epidemiology

TB is one of the most prevalent diseases in the world. About ***1/3*** of the world's population is infected é TB & thus at risk of developing active disease. It is estimated that 8.4 million people develop active TB every year & 2.3 million die. **>**90% of TB cases & deaths occur in developing countries & 75% of those are in the most economically productive age group. Not everyone exposed becomes infected, the probability of transmission depends on many factors as:-

*Infectiousness.

*Type of environment.

*Length of exposure.

Most people who are exposed to TB never develop symptoms because the bacteria can live in inactive form in the body. But if the immune system weakens,

such as people é HIV or elderly adults, TB bacteria can become active. In their active state, TB bacteria cause death of tissue in the organs they infect. The active TB disease can be fatal if left untreated. 10% of infected persons will develop TB disease at some point in their lives. Coinfection é HIV significantly ⇧ the risk of developing active TB. HIV has become the most important risk for developing active TB. In HIV-infected persons, the risk of developing TB ⇧ by >10 times compared to those who are HIV -ve. The incidence & prevalence of TB, in recent years has doubled or tripled because of the HIV pandemic, especially in developing countries. It is also shown that active TB can result in rapid progr-ession of HIV infection in a pt. Multi-drug resistant TB, ẃ often results from poor management is becoming a serious concern in many countries.

Transmission

Adults é smear +ve TB (cavitory & laryngeal) are sources of infection. Pts who are culture -ve pulmonary TB or é extrapulmonary TB are not infectious. M. tuberc-ulosis is commonly transmitted from a pt é infectious TB to a healthy individual through:- inhalation of droplets excreted via coughing, sneezing. Unboiled milk could also transmit M. bovis but the incidence seems to ⇩ because of health edu-cation on boiling or pasteurizing milk.

Factors facilitate transmission

- Infectivity of the contact (pt é heavy bacterial load).
- Overcrowding.
- Prolonged exposure.
- Intimacy (how close the subject are). Pts who acquire the infection may not develop the disease. The rate of clinical disease is highest during late adolescence

& early adulthood, but the reasons are not clear, especially young women > men.

Diseases ⇧ the risk of TB

•The commonest is HIV, ẃ suppresses cellular immunity •Hematologic & other malignancies as lymphoma & leukaemia •DM, CRF, immunosuppressive drugs like long term steroids •Old age because of ⇩ immunity & malnutrition.

Pathogenesis

M. tuberculosis enters the body mostly via resp. tract through coughed out droplets from an infectious pt. Interacts é host immune system immediately after entry. The activated alveolar macrophages ingest the bacilli; after ẃ they release chemicals to activate other immune system components & try to control the infection or multiplication of bacilli. This process will bring about cell-mediated immune response. These activated cells (macrophages) aggregate around the lesion & the center becomes necrotic, soft cheese like material called caseous necrosis. The center, however, may still contain live bacteria that become dormant. These bacteria will flare up & multiply when the person's immunity is depressed. But if bacteria inside the macrophage multiply rapidly, they will kill the macrophage & are released but to be taken up by other macrophages again. If this process is not arrested, pt. may develop disseminated infection.

Clinical manifestations

Primary pulmonary TB

Clinical illness directly after infection is called primary TB; this is common in children < 4 yrs of age. Thus, it results from an initial infection. Frequently it involves the middle & lower lung zones. In the majority it heals spontaneously leaving a healed scar on the lung called Ghon lesion. It may be contained by im-

munity into dormant stage only to flare up in immunocompromised state. In children or immunocompromised individuals the disease is usually rapid involving the lungs, pleura & mediastinal LNs. It may disseminate into the blood stream causing milliary TB or TB meningitis that may be rapidly fatal.

Secondary pulmonary TB

If no clinical disease developed after the 1ry TB infection, dormant bacilli may persist for yrs/decades before being reactivated, when this happens, it is called 2ry TB. Therefore this is from endogenous reactivation of latent infection, is more common in adults & typically involves the apical lobes. But any portion of lungs may be involved. The disease extend from small infiltrates to large cavitory lesions. Pt é cavitory lesion expectorate the TB bacilli é sputum. Early in the course, the pt. may have intermittent fever, night sweats, wt loss, anorexia & weakness. Most pts have cough, ẃ may be dry at first & later becomes productive, it is frequently blood streaked & pt may have exercise dyspnea.

Physical examination

May reveal a chronically sick pt. é pallor & clubbing. Inspiratory crepitations seen in some cases.

Laboratory findings

May include ⇧ ESR, anaemia or leucocytosis. Sputum examination may be +ve for AFB. The CXR findings are non-specific; infiltrations, consolidation or cavitory lesions may be present.

Extra-Pulmonary TB

Commonly affected organs are: LNs, pleura, meninges, genitourinary tract, bones, joints & peritoneum, each will be discussed separately:-

Tuberculous Lymphadenitis

Seen more in HIV pt, commonest sites are cervical & supraclavicular. LNs typically matted, firm & sometimes discharging pus. Diagnosis is made by fine needle aspiration or biopsy.

Pleural Tuberculosis

May be asymptomatic or pt. could have fever, pleuritic chest pain & dyspnoea. On physical examination, typically there will be ⇩ tactile fremitus, dullness & ⇩ breath sounds on the affected side. Fluid should be aspirated from pleural space & analysed. CXR is helpful, it may show homogenous opacity é meniscus sign. Empyema (pus in the pleural space) may complicate pleural TB.

Genitourinary Tuberculosis

Affects more females & may present as infertility or pelvic pain. Can involve any part of genitourinary system. Dysuria, intermittent hematuria & flank pain are common presentations. But it may be asymptomatic for a long period of time. Urine analysis shows pyuria & hematuria éout bacteria in majority of cases (commonly called sterile pyuria). Diagnosed by culturing urine repeatedly.

Skeletal Tuberculosis

It is usually reactivation of haematogenous site or extension from a nearby LNs. Most common sites are spine, hips & knees.

Spinal Tuberculosis

“Pott's disease” or “TB spondylitis”. In adults, lower thoracic or lumbar vertebrae commonly affected. Pt present é swelling & pain on the back é/éout paraparesis or paraplegia due to cord compression. TB in other bones usually present é pain & swelling. Any joint can be affected but weight bearing joints; particularly hip &

knee are commonly involved. Pt present é progressive joint swelling usually é pain & limitation of movement & if left untreated, joint may be destroyed.

Tuberculous Meningitis

Commonly seen in children & immunocompromised people. 50% of cases have evidence of disease in the lungs. AFB can be seen in CSF sediment in only 20% of cases; this % ⇧ if the examined CSF volume is increased. The culture may be +ve in 80% of cases, but it takes 4-6 wks to grow.

Gastrointestinal Tuberculosis

Can affect anywhere from the mouth to the anus. Bacteria could reach GIT by swallowing sputum, or through blood, or ingesting raw milk. The commonest sites to be involved are terminal ileum & cecum. Abdominal pain, diarrhea, symptoms of intestinal obstruction & hematochezia (frank blood on stool) may be the presenting symptoms. There could be associated fever, night sweats, wt loss & anorexia. There could be a palpable mass in abdomen. Pt could have involvement of peritoneum, liver & spleen. TB peritonitis arises from ruptured abdominal LNs, or through blood. Pt usually presents é abdominal swelling & pain, wt loss, fever & night sweating. Aspiration of peritoneal fluid (paracentesis) reveals exudative fluid é many WBC, predominantly lymphocytes. AFB is rarely +ve & culture positivity is very low. Involvement of the liver & spleen are parts of disseminated TB & the pt will present é hepatomegaly &/or splenomegaly. There may be evidence of other organs involvement.

Tuberculous Pericarditis

Frequently seen in pt é HIV. Pt usually present é fever, retrosternal pain, cough, dyspnea & generalized oedema. Cardiac tamponade may appear later. Constrict-

ive pericarditis may develop as complication even after Rx & pt can present é symptoms & signs of RHF. Diagnosis usually reached by analysing the pericardial effusion. It may show lymphocytosis, but yield for AFB is low. The CXR may show cardiomegaly (pericardial effusion). ECHO (detect effusion).

Milliary Tuberculosis

This is secondary to haematogenous dissemination of the bacilli. More common inchildren & immunocompromised pt. The manifestations of military TB are nonspecific é fever, night sweat, anorexia, weakness & Wt loss ± respiratory symptoms. Physical examination findings includes; seriously sick pt é hepatosplenomegaly & lymphadenopathy. Since symptoms & signs are not specific, high index of suspicious is required for the diagnosis. CXR usually shows milliary infiltration bilaterally.

Diagnosis of Tuberculosis

Clinical suspicion very important, pt who have suggestive symptoms & signs for TB should undergo further tests including the following:-

AFB Microscopy: AFB is found on microscopy from specimens like sputum, pleural, peritoneal, CSF & body discharges, but the yield is different. However, definitive diagnosis depends on detection of M. tuberculosis from a culture of specimen.

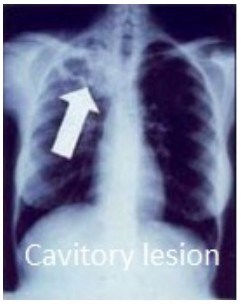
Sputum examination: is extremely important in pt who have sputum production . AFB stain should be done 3 times in 2 consecutive days (spot-early morning). Sputum smear is said to be +ve when at least 3 AFB are seen. Or smear +ve TB is diagnosed when 1-2 smears are +ve plus suggestive CXR finding. If all 3 sputum smears are -ve & the pt has suggestive clinical & CXR findings, first the pt should

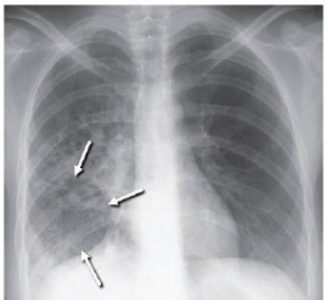
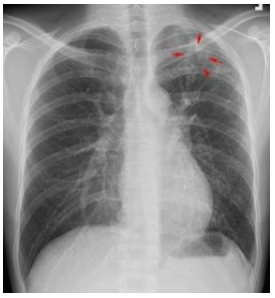
treated é broad spectrum antibiotics to R/O other bacterial causes. If the pt does not respond, smear -ve pulmonary TB can be strongly considered.

Mycobacterial culture: gold standard for diagnosis. However the bacillus is slowly multiplying, it takes several wks. to grow the bacilli in a culture media. May be used for drug sensitivity tests.

Chest X Ray

Presentations are varied. Although any CXR finding is possible, typically there will be nodular infiltrates & cavities in the upper lobe; pleural effusion is also common. But CXR findings alone do not confirm diagnosis.



Raised ESR: very important clue for diagnosis even though this is nonspecific.

PPD skin test: widely used to screen TB in developed countries where the prevalence of TB is low. Positive reaction obtained when pt have the infection but do not have active disease or they have received BCG for immunization.

Mantoux tuberculin skin test: 0.1 mL/5u of purified protein derivative solution is injected ID, use a 27 gauge needle. Read within 48-72 hrs, measure induration, not erythema. A +ve reaction can be measured accurately for up to 7 days. A -ve reaction can be read accurately for only 72 hours.

Interpretation of TST is as follow:-

5 mm of induration is +ve in:- HIV-infected persons, or close contacts to an infectious TB case, or in persons who have CXR findings consistent é prior

untreated TB, or organ transplant recipients, or persons who are immunosuppressed (e.g. those taking the equivalent of >15 mg/day of prednisone for 1 month).

False +ve reaction: non-tuberculous mycobacteria: induration are usually ≤ 0 mm. BCG vaccination: generally wanes over time.

No reaction: anergy, or inability to react to TST due to weak immune system, or recent TB infection (2-10 wks after exposure), or very young age (newborns), or recent live-virus vaccination (temporarily suppress TST), or poor TST administration technique (too shallow or deep).

Standardized case definition of TB

After making diagnosis of TB proper case definition should be made to decide on appropriate Rx. Definition of TB case depend on the following points:-

①Site of TB (Pulmonary Vs Extrapulmonary).

Pulmonary TB: refers to disease involving lung parenchyma. Therefore tuber-c u l ous intrathoracic lymphadenopathy (mediastinal or hilar) or tuberculous pleural effusion, éout radiographic abnormalities in the lungs, constitutes a case of extra-pulmonar TB. Pt. é both pulmonary & extra pulmonary TB should be classified as a case of pulmonary TB. Milliary TB is classified as pulmonary TB because there are lesions in the lungs.

Extrapulmonary TB: refers to TB of organs other than the lungs, e.g. pleura, LNs , abdomen, genitourinary tract, skin, joints, bones, meninges. Diagnosis based on one culture +ve specimen, or histological or strong clinical evidence consistent é active extra-pulmonary TB, followed by decision by a clinician to treat é a full course of TB chemotherapy. The case definition of extra-pulmonary TB case é several sites affected depends on the site of the most severe form of disease.

②Bacteriology (sputum smear)

Identification of smear +ve cases is important, because they are the most infectious cases & usually have higher mortality.

Pulmonary TB +ve sputum smear: ≥ 2 initial sputum smear examinations are +ve for AFB or 1 sputum smear +ve & CXR abnormalities consistent é active pulmonary TB as determined by a clinician, or 1 sputum smear +ve & sputum culture +ve.

Pulmonary TB -ve sputum smear: case of pulmonary TB that don`t meet the above definition for smear +ve TB. This group includes cases éout smear result, ẃ should be exceptional in adults but relatively more frequent in children.

Note: in keeping é good clinical & public health practice, diagnostic criteria for pulmonary TB should include:- at least 3 sputum specimens -ve for AFB & CXR abnormalities consistent é active pulmonary TB & no response to a course of broad spectrum TB antibiotics & decision by Dr to treat é a full course of anti TB chemotherapy. In health facilities where microscopy laboratory services available & diagnostic criteria are properly applied. Pulmonary TB smear +ve cases represent at least 65% of the total of pulmonary TB cases in adults.

Note: these proportions may be lower in high HIV-incidence populations. It is app arent from the above definitions that in the absence of culture positivity, the standard CXR is necessary to document cases of smear -ve pulm. TB.

③History of previous Rx of TB

In order to identify those pts at ⇧ risk of acquired drug resistance & to prescribe appropriate Rx, a case should be defined according to whether or not the pt has previously received TB Rx. Pt may be new case, or relapse after cure, or failure of present Rx, or é interruption of Rx for ›2 months, or pt transferred from another

TB register to continue Rx, or sputum +ve pt at the end of Rx regime, or ch. case.

④Severity of the diseases

Bacillary load, extent of disease & anatomical site are considerations in determining TB disease severity & therefore the appropriate Rx. Involvement of an anatomical site results in classification as severe disease if there is a significant acute threat to life (e.g. pericardial TB), a risk of subsequent severe handicap (e.g. spinal TB).

Management

Initial phase			Continuation phase		
eg	Drug	Duration	Reg	Drug	Duration
1	INH RIF PZA EMB	7 days/week for 8 wks or 5 days/wk for 40 doses	1a 1b 1c	INH/RIF INH/RIF INH/RPT	7 days/wk for18 wks or 5 days/wk for 18 wks twice weekly for 18 wks Once weekly for 18 wks
2	INH RIF PZA EMB	7 days/wk for 2 wks then twice weekly for 12 doses. or 5 days/wk for 2 wks then twice weekly for 6 wks	2a 2b	INH/RIF INH/RPT	Twice weekly for 18 wks Once weekly for 18 wks
3	INH RIF EMB	Three times weekly for 8 wks	3a	INH/RIF	3 Times weekly for 18 wks
4	INH RIF EMB	7 days/week for 8 wks or 5 days/ week for 8 wks	4a 4b	INH/RIF INH/RIF	7 days/wk for 31 wks or 5 days/week for 31 wks Twice weekly for 31wks

The aim of treatment

- To cure pt, prevent death & complications.
- To ⇩ transmission of TB.

The intensive phase

Combination of ≥ 3 or more drugs is given for 2 months using the (DOTS). In the retreatment regimen DOTS is continued for 3 months, to ⇩ the bacterial load & make the pt non-infectious rapidly.

Continuation phase

2-3 drugs used for 4-5 months . This phase follows the intensive phase & the aim is to achieve complete cure.

•Streptomycin should not be given to pregnant woman or pt é RF, or ear proble-ms. It should be replaced by Ethambutol. The dose of streptomycin should not be >750 mg if the pt's age >50 yrs.

Case definitions

TB suspect: any person who presents é symptoms/signs suggestive of TB, in particular cough of long duration (›2 wks).

TB Case: TB has been bacteriologically confirmed or diagnosed by a clinician.

Definite case of TB: +ve culture for the M.TB complex.

Important points

•Children ≤ 6 yrs old should not be given Ethambutol because of damage to the eyes & children may not complain of it.

•Pts should be strictly followed after initiation of the drugs.

•All sputum +ve pts. on DOTS must have one sputum specimen examined at the end of the 2^{nd}, 5^{th} & 7^{th} month.

- Steroids are added in case of TB meningitis, pericarditis & spinal TB.
- If sputum is -ve at the end of 8 wks, the continuation phase can be started.

Side effects of Anti TB drugs

Drug	Common side effects
Isoniazide	Peripheral neuropathy, Hepatitis, Histamine release after ingestion of red fish e.g. Bala, Kelawalla
Rifampicin	Nausea, Vomiting, Hepatitis, reduced effect of contraceptives, anti-epileptics, oral hypoglycaemic drugs & Theophillines
Pyrazinamide	Joint pain, Hepatitis
Streptomycin	Audio & Vestibular damage, (also to the foetus), renal damage
Ethambutol	Optic neuritis

MENINGITIS

Inflammation of the arachnoid layer of the meninges & the fluid that circulates in the ventricles & subarachnoid space (CSF).

Etiologic agents

The causes of bacterial meningitis vary é age:-

Severe skin & systemic infection of baby born after prolonged rupture membrane for several days, baby was very foul smelling, skin desquamating & erythematous ē evidence of fissuring, culture of skin swab shows growth of E coli, group B streptococci, staphylococcus aureus or candida albicans. The commonest organism in the NN period is group B streptococci & E coli, then come gram -ve bacteria. 10% of pregnant mothers are found to be colonized in vagina ē group B streptococci & 25% of their babies found to acquire this bacteria, mortality rate of neonatal sepsis is 20-80%, surviving infants may have significant neurologic squeals. Bacteria gain access into the blood stream, may cause overwhelming infection ēout much localization (septicemia) or may get localized to lung (pneumonia) or meninges (meningitis). Early onset sepsis presenting in 1st wk of life, through organisms in mother genital tract or in delivery room (nosocomial infection), commonly associated ē LBW, PRM, chorioamnionitis, foul smelling liquor, difficult or prolonged labor, meconium aspiration syndrome, maternal infection during pregnancy & often manifest as pneumonia, less commonly septicemia or meningitis.

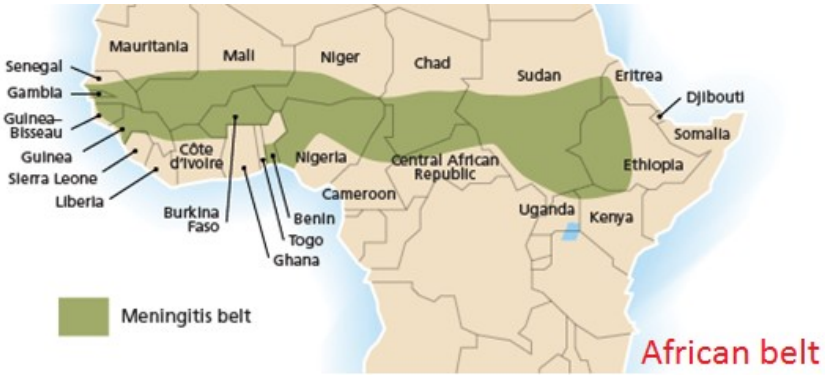
Late onset sepsis is presenting after 1st wk of life, result from acquired infection from home or hospital, hands of care providers, present ē septicemia, pneumonia, or meningitis, commonly associated ē LBW, lack of breast feeding, superficial skin infection (pyoderma), home deliveries especially in rural areas, traditional practices as circumcision away from hospital, umbilical sepsis, aspiration of feed, disruption of skin integrity ē needle pricks & use of IVFs.

- **Infants (<1 yr):** E. coli, B strept & Listeria monocytegenous are the commonest.
- **Young children/toddlers (age 1-6 yrs):** Haemophilus influenza & Meningococcus account for **>** 50% of cases.
- **Adolescents/Adults:** Meningococcus & Pneumococcus are the commonest.
- **Immunocompromised & cancer pts:** Listeria, Staphylococcus & Pseudomonas.

Rout of infection

- **Droplet infection through the upper airways:** e.g. in meningoccus meningitis, é possibly epidemic spread.
- **Haematogenous spread:** e.g. in pneumococcus pneumonia.
- **Contagious spread from adjacent sites:** e.g. otitis media, or sinusitis.
- **Direct:** e.g. in open head injury.

Epidemiology of Meningococcal Meningitis



In the west due to the availability of vaccines for N. meningitides & H. influenza,

the S. pneumonia has become the leading cause of bacterial meningitis. However ,in African & most developing countries, Neisseria meningitidis is still the leading cause of bacterial meningitis in adolescents & adults. An outbreak of meningitis epidemic has been documented to occur every 7-10 yrs in the meningitis belt in Africa. Neisseria meningitidis, often referred to as meningococcus, is a gram -ve bacterium that can cause meningitis & other forms of meningococcal disease such as meningococcemia, a life-threatening sepsis. The bacterium is referred to as a coccus because it is round & more specifically, diplococcus because of its tendency to form pairs. About 10% of adults are carrier of the bacteria in their nasopharynx. As an exclusively human pathogen it is the main cause of bacterial meningitis in children & young adults, causing developmental impairment & death in about 10% of cases. It causes the only form of bacterial meningitis known to occur epidemically, mainly in Africa & Asia. N. meningitidis is spread through saliva & respiratory secretions during coughing, sneezing, kissing & chewing on toys.

Clinical presentation

In infants: mostly vague, in early onset sepsis the baby may presented ē RD, apneic spells or gasping, may be the only manifestation of septicemia. Hypothermia is common & fever is infrequent. Lethargy, inactive & reluctant to feed. In late onset sepsis the baby, ,who had been active & sucking well, gradually or suddenly, become lethargic, inactive, refuse sucking, may presented ē diarrhea, vomiting, abdominal distension, poor capillary perfusion, jaundice, sclerema. Critical neonate may develop shock, cyanosis, bleeding & renal failure. With meningitis baby develop irritability, high pitched cry, excessive crying, seizures,

blank look, neck retraction, bulging fontanel, focal neurological signs.

Meningococcal meningitis

The IP for meningococcal meningitis range from 1-10 days, but mostly the clinical manifestations occur within 2-4 days. Meningitis may manifest as an acute fulminant illness that progress rapidly in few hrs or as a subacute infection that progressively worsens over several days. The classic clinical triad of Fever, Headache, Nuchal rigidity (neck stiffness) is seen in >90% of pts. Alteration in mental status can occur in >75% of pts & can vary from lethargy to coma. Nausea &vomiting are common symptoms. Avoiding light (photophobia) seen in some pts. Seizures occur as part of the initial presentation of bacterial meningitis, or during the course of the illness in 20-40% of pts. In Meningococcal meningitis of sudden onset é severe course, pt. develop diffuse erythematous maculpapular rash ẃ rapidly becomes petechial, purpural or bullous lesions. The petechiae are found on the trunk, lower extremities, in m.m., conjunctiva & occasionally on the palms & soles. In older/debilitated pt meningitis symptoms may be subtle.

Meningococcal rashes

Meningeal signs

Are clinical signs often sound in pt é meningitis, include:-

Neck stiffness: when head is flexed passively.

Brzezinski's sign: upon passively flexing the head, one notices flexion of both legs at the knees.

Kerning's sign: severe stiffness of hamstrings muscles causes an inability to straighten the leg when the hip is flexed to 90^0.

Note: these classic meningeal signs may not be seen in infants, or old persons & in case of the pt is in coma.

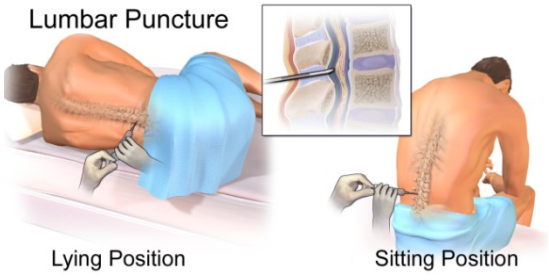
Complications

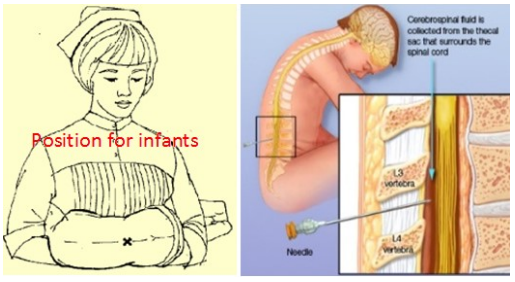
•Brain oedema. •Hydrocephalus. •Brain abscess. •Septic vein thrombosis. •Hearing impairment. •Fulminant meningococcal sepsis: Water-house-Friedrichsen syndrome (a clinical condition resulting from hemorrhagic necrosis of the adrenal gland é multiorgan failure. Pts are hypotensive or in shock, DIC é skin & mucosal purpura & bleeding are commonly seen associated features.

Diagnostic approach

•History, physical examination. •Search for possible source of infection (pneumonia, otitis media, sinusitis). •Blood culture; meningococcus are seen as gram -ve intracellular diplococcic. •PCR, serologic antibody test: latex agglutination test. •Lumbar puncture.

Technique of lumbar puncture





Feel the upper border of iliac crest it's at the level of L5 vertebrae, go up to touch

spine of L4 vertebrae & under complete aseptic conditions introduce needle (size FG 21, 22, for infants &children) into the disc space between L4-L3 vertebrae, dire- cting the needle towards the umbilicus, if CSF was found to come out under high pressure stop the procedure to avoid conning of cerebellum. Collect CSF in 3 tub-es, 10 drops in each for cells, biochemistry & culture. Take blood sample for BS after you finish to compare é CSF sugar (normally the CSF sugar is ‹2/3 of blood sugar), ⇩ CSF sugar seen in bacterial meningitis.

CSF analysis

Gross appearance & opening pressure: CSF looks turbid &the opening pressure is⇧ (due to ⇧ICP).

Cell count/µl & differential: polymorphonuclear leucocytosis (several thousands in bacterial & several hundred in viral or TB. meningitis).

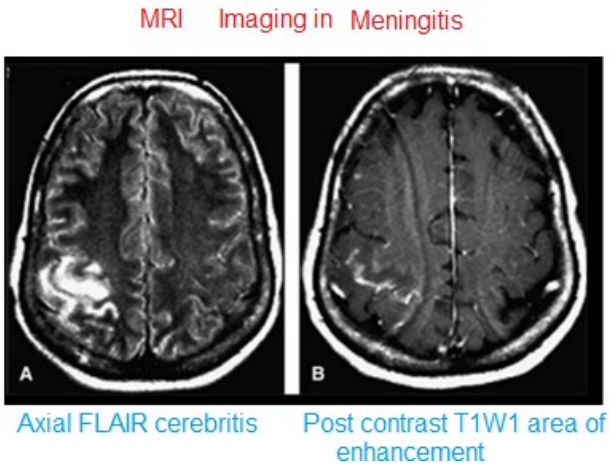
Cell type: granulocytes (PMNLs) in bacterial meningitis. Lymphocytes (viral meningitis). Lymphocytes + Monocytes (seen é TB. meningitis).

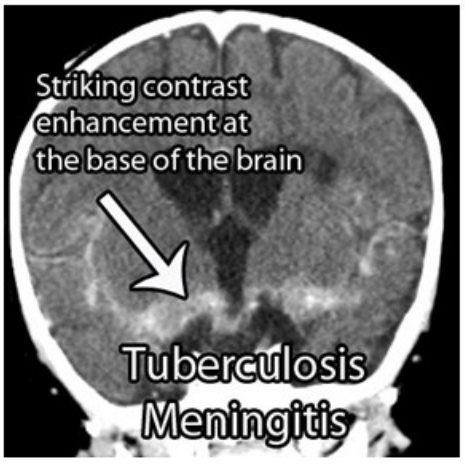
Protein& Glucose: ⇩ glucose & ⇧ protein (bacterial meningitis).

Gram stain culture/sensitivity: for identification of type of bacteria.

Parameter	Normal	Bact Meningitis	Viral Meningitis	Fungal Meningitis	Tuberculosis
Opening pres. (mm H_2O)	<180	200-500	NA	> 250	NA
WBC count (mm^3)	0-5	100-20.000 (mean 800)	5-500 (mean 80)	20-2000 (mean 100)	5-2000 (mean 200)
WBC Differen,	No predominance	> 80% PMN	> 50% L < 20% PMN	> 50% L	> 80% L
Protein (mg/dL)	15-50	100-500	30-150	40-150	> 50
Glucose (mg/dL)	45-100 (2/3 of serum)	<40 (<40% of serum)	30-70	30-70	< 40
Gram stain	NA	60-90% +ve	-	-	37-87% +ve (AFB smear)

Imaging in Bacterial Meningitis





Neuroimaging can identify conditions that may predispose to bacterial meningitis ;thus, it is indicated in pts who have evidence of head trauma, sinus or mastoid infection, skull fracture &congenital anomalies. In addition, neuroimaging studies are typically used to identify & monitor complications of meningitis, such as hydrocephalus, subdural effusion, empyema, infarction & to exclude parenchymal abscess & ventriculitis. Identifying cerebral complications early is important as some complications, as symptomatic hydrocephalus, subdural emp-yma &cerebral abscess, require prompt neurosurgical intervention. The diagnosis of acute bacterial meningitis is not made on the basis of imaging studies. Rather, it is established by the affected pt's history, physical examination findings & laboratory results. The CSF is the single most important diagnostic study. Imaging studies performed in pt. é acute meningitis may provide normal findings. The results of an imaging study do not exclude or prove acute meningitis.

Differential Diagnosis

•Virally caused Meningoencephalitis: Coxsackie, Mumps, Measles, HIV, CMV, VZV, HSV. •Chronic meningitis: TB/Cryptococcal. •SAHge.

Treatment:

1. Empirical antibiotic therapy: bacterial meningitis is a medical emergency & antibiotics should initiated immediately before results of CSF gram stain/culture. Antibiotics should be given IV at higher doses. In adults éout underlying disease; Ceftriaxone 2 gm IV BID **+** Ampicillin 2 gm IV QID for 2 wks. Crystalline penicillin 3-4 million u, IV/4 hrs **+** Chloramphenicol 1 gm IV QID are alternative for a resource limited setting. Pts é ENT infection or head injury: we use Ceftriaxone 2gm IV BID **+** Vancomycin 1 gm IV BID **+** Rx of the underlying cause. If suspected hospital-acquired infection; Ceftriaxone 2 gm IV BID **+** Vancomycin 1 gm IV BID + Gentamycin 80 mg TID. In case of immunodeficient pt we use: Ceftriaxone 2 gm IV BID **+** Vancomycin 1 gm IV BID **+** Ampicillin 2 gm IV QID (Ceftriaxone is 3rd gen. Cephalosporine & Vancomycin is Aminoglycoside).

2. Specific antibiotic therapy: when specific agent identified:-

N. meningitidis: 3rd gen. Cephalosporin e.g. Cefotaxime provide adequate empirical coverage, Penicillin G remains the drug of choice for N. meningitides, 3-4 million U, IV/4 hrs for 7-10 days may be adequate.

Pneumococcal meningitis: antibiotic Rx is initiated é Ceftriaxone 2 gm IV BID & Vancomycin 1 gm IV BID for 2 wks.

H. influenza: Ceftriaxone 2 gm IV BID for 10-14 days may be enough. Chloram-phenicol 1 gm IV QID may be an alternative, antibiotic, for pts who may not afford Ceftriaxone.

Viral meningitis : Antiviral inhibit viral duplication in case of H. Simplex, H. Zoster ,Varicella, EBV or CMV infection. Zovirax sy 200 mg. For children 6 month -12 yr give 200 mg X 3 X 5 day or amp 250 mg infusion over over 1 hr/8 hr for 5 days. Or

Acyclover amp 250 mg, 15 mg/Kg /day ÷ 3, IV over 1 hr for 10 days.

Tuberculous meningitis: Rifampicin amp 250 mg IM, dose 20mg/Kg/day÷ 2 for 2 wks + Streptomycin 1000 mg amp , 25 mg/Kg/day ÷2, IM for 2 weeks. Or Rifam plus cap (Rifampicin + Isoniazide) 150 /100 for children, for 7 months if sputum is +ve for AFB.

Symptomatic & Adjunctive therapy

Steroids: Dexamethasone when initiated be- before antibiotic therapy ⇩ the number of unfavourable outcomes, including death & neurologic complications. It is mainly advantageous in children, predominantly é meningitis due to H. influenza or St. pneumonias. 10 mg IV 15-20 min. before the first dose of antibiotics & 4 mg IV QID for 4 days.

Treatment of ⇧ ICP: elevation of the pts head to 30-45^0. Intubation & hyperventilation (till P_aco_2 is 25-30 mmHg). Mannitol IV infusion.

Isolate the patient

Regulate water, electrolyte balance, thromboembolism prophylaxis.

Chemoprophylaxis

In case of *N. Meningitides,* all close contact to the pt should be given chemoprophylaxis:- Rifampicin 600 mg PO BID for 2 days for adults & 10 mg/ kg PO BID for children >1 yr. Ciprofloxacin 750 mg PO stat, may be given as alternative (adults). Vaccinate all children age 1-5 yrs whom are in hospital & to all health workers in hospital, or give Rifampicin syrup 100 mg, dose of 20 mg/Kg/day ÷ 2 for 2 days

Neonates

Meningitis Septicaemia/Pneumonia

Antibiotic	Dose	Frequency/Age <7 days	Frequency/Age >7 days	Route	Duration
Ampicillin or Penicillin or	100 mg/Kg /day 1000.000 U/Kg/D	12 hrly 6 hourly	8 hrly	IV, IM IV, IM	7-10 days
Cloxacillin +	100 mg/Kg /day	12 hrly	8 hrly	IV	7-10 days
Gentamicin or	3-5 mg/Kg /day	12 hrly	8 hrly	IV, IM	7-10 days
Amikacin	7.5 mg/Kg /day	12 hrly	8 hrly	IV, IM	7-10 days

Ampicillin +	100 mg/Kg/day	12 hrly 8 hrly	IV	3 weeks
Gentamicin or	3-5 mg/Kg/day	12 hrly 8 hrly	IV	3 weeks
Claforan +	50 mg/Kg/day	12 horly	IV, IM	10 days
Vancomycin	50 mg/Kg/day	12 horly	IV, IM	10 days

INFECTIOUS DISEASES MENINGITIS

- Anticonvulsant: Valium amp 5, 10 mg, 0.25 mg/Kg/dose stat IV or IM, suppository 5, 10 mg, daily maintenance is 0.25 mg/Kg/day÷4.

Phenobarbital amp. 200 mg, syrup 20 mg, first dose is 15 mg/Kg IV or IM, maintenance 5 mg/Kg/day÷2-4.

Epanutine amp 250mg, syrup 30mg, starting dose 15mg/Kg, maintenance 5mg/Kg/day÷4.

- Vit. K 1mg IM (to guard against bleeding).
- Oxygen by hood or mask, if baby cyanosed, grunting, or distressed.
- Gentle physical stimulation, if baby apneic.
- Dexamethasone in case of septic shock, 0.5 mg/Kg/dose, IV, 6 hourly for 2 days.
- Exchange transfusion may be needed if there is sclerema.
- There is no role of immunoglobulin's therapy in neonatal sepsis.

VIRAL ENCEPHALITIS

Inflammation of the brain parenchyma, é/éout involvement of the meninges, caused by virus. The spinal cord &/or nerve roots may be involved rarely.

Causes

•Common: Arbovirus. Enterovirus, HSV-1, Mumps. •Less common: CMV, EBV, HIV, Measles, VZV. •Rare: Adeno V, CTFV, Influenza A, Rabies, Rubella.

Signs & symptoms

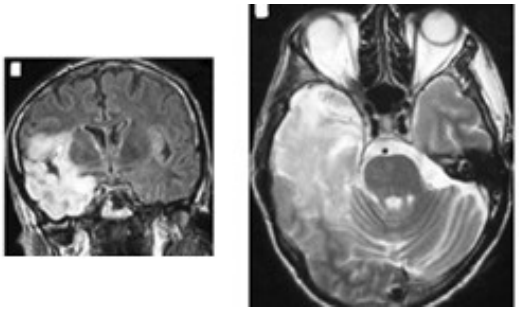
Acute febrile illness é evidence of meningeal involvement. Altered level of consciousness (ranging from lethargy to coma). Abnormal mental state (hallucinations, agitation, personality change, psychosis). Evidence of either focal or diffuse neurologic signs/symptoms. Focal or generalized seizures occur in >50% of cases.

Most common focal findings: aphasia, ataxia, hemiparesis (é hyperactive tendon reflexes), involuntary movements & cranial nerves palsy.

Laboratory findings

CSF examination: check for ⇧ ICP first. The characteristic profile of CSF consists of lymphocytic pleocytosis,⇧ protein & normal glucose level. CSF PCR. CSF culture usually -ve (especially in HSV-1) .

Serologic studies & antigen detection. **MRI, CT & EEG:** done to exclude alternative diagnosis & assist in differentiation between focal & diffuse encephalitic process (90% of pts é HSV-1 infection have abnormalities in temporal lobe on MRI).



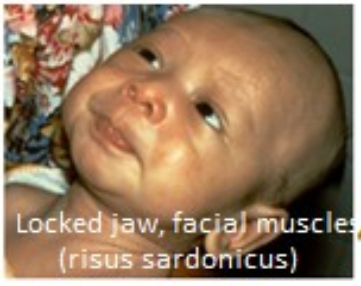
MRI brain(T2W image) right temporal lobe high signal in a pt with herpes encephalitis

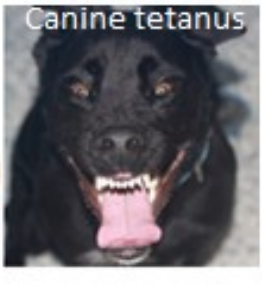
Treatment

Supportive Rx (usually in ICU): check vital signs, restrict fluid & give antipyretics. Treat seizures/or give prophylactic therapy (high risk for seizures!).

Medication: Acyclovir 10 mg/kg TID for at least 14 days (for herpes). Gancyclovir (5 mg/kg BID) or Foscarnet (60 mg/kg TID) are especially recommended for CMV.

TETANUS





Neurologic disease characterized by ⇧ muscle tone & spasms caused by toxin rele- ased from the bacteria clostridium tetany. it is spore forming anaerobic, motile & rod shaped. Forms oval, colorless, terminal spores (tennis racket or drumstick shape), spores are very resistant to heat, chemicals, radiation, drying & can survive for long time in environment (months up to yrs, decades), it is found worldwide in soil, in inanimate environment, in animal, faeces, skin surfaces, contaminated substances including heroin. Disease occurs sporadically, affects unimmunized, or partially immunized, or fully immunized who fail to maintain adequate immunity é booster doses of vaccine. Tetanus Neonatorum is caused through an unvaccinated mother, or é home deliveries & unhygienic cutting of umbilical cord. It is common in the 3rd world countries as a result of the high % of home deliveries & lack of vaccination & poor sanitary conditions, causing several hundred thousand deaths/ yr. Tetanus caused by exotoxin produced by the G +ve

bacteria Clostridium tetany ẃ produces 2 exotoxins; tetanolysin; its action not known & tetanospasmin ẃ is neurotoxin bind to CNS interfering é the neuro-transmitter release to block inhibitor impulses causing the clinical manifestations of the disease.

Epidemiology

Tetanus is more common in rural areas where there is frequent contact é soil. Occurs more frequently in warmer climates, during summer months & in males. Most cases follow injuries especially during farming, gardening or other outdoor activities. Tetanus may also be associated é surgery, otitis media, abortion, home deliveries, or canine tetanus (dogs, wild animals).

Pathogenesis

Although Cl. tetany frequently contaminates wounds. Germination & toxin production, however, takes place in wounds é necrotic tissue, foreign bodies or infection that is active. Often the wound is trivial or could seem to be healed from outside. Tetanospasmin: toxin produced by the bacteria in the wound binds to peripheral motor neuron terminals, enters the axon & is taken to spinal cord & brain stem by retrograde transport. Toxin then inhibits release of inhibitory neurotransmitter & GABA é diminished inhibition, there will be ⇧ excitation, spasm & rigidity. Tetanospasmin may also block neurotransmitter release at the neuromuscular junction producing weakness or paralysis. Generalized tetanus occurs when toxin enters into blood stream & lymphatic to affect distant nerve endings.

Clinical Manifestations

The IP (time between injury & 1st symptom) of tetanus is about 7-10 days but it may range from 1 day to 2 months. The period of onset (time between the first

symptom & spasm) ranges 1-7 days. The shorter the IP & period of onset, the more severe the disease becomes. There are different forms of tetanus:-

Generalized Tetanus

Is the most common form. The median time of onset after injury is 7 days; but could occur as early as within 3 days. Usually the first symptom is ⇧tone in masseter muscle (trismus, or lock jaw) & pt. is unable to open his mouth. Immediately after this the pt. develops dysphagia, stiffness in the neck & back. Then the pt develops contraction of facial muscles to produce rhesus sardonicus (sneer or grimace). There may be arched back (opisthotonos). Generalized muscle spasm triggered by stimulus such as light, noise, or touch. The deep tendon reflexes may be exaggerated & there may be dysphagia or paralytic ileus.

Localized tetanus

Rare form of tetanus. Presents é rigidity & spasm around the portal of entry. While most localized tetanus have good prognosis, cephalic tetanus has high mortality, comes after head/or face injury or ear infection. Pt may come é wide ranges of wound severity, although most have trivial or healed wound. In fact 20% of pts may not give history of injury.

Neonatal tetanus

Occurs in NN of non-immunized mother & those delivered in unhygienic conditi-on. It is a very severe form of tetanus é **>** 90% mortality. NN should referred urge-

ntly to a nearby hospital if there is suspicion of clinical tetanus. NN tetanus presents most often after the 7th day of life (IP) é short history of failure to feed. Spasms are typical but the diagnosis can be mistaken for meningitis or sepsis. NN present é generalized rigidity, painful, paroxysmal convulsions, spasm of voluntary muscles involving; masseters (lock jaw), facial muscles (risus sardonicus), muscles of back & neck (opisthotonos position), difficult swallowing & fever in 40% of cases. The NN consciousness is retained. Tetanus may be graded according to severity into the following grades:-

Grade I (mild): mild trismus, mild spasticity.

Grade II (moderate): moderate trismus, moderate & short lasting spasms, tachypnea (RR 30-35/min) & mild dysphagia.

Grade III (severe): severe trismus, generalized spasticity, resp. embarrassment (RR >40/min), apnoeic spells, tachycardia (>120/min) & severe dysphagia.

Grade IV (very severe): features of grade III **+** severe autonomic disturbance of CVS, including episodes of hypertension & tachycardia alternating é relative hypotension& bradycardia or sever persistent hypertension (DBP >110 mmHg) or hypotension (SBP <90 mmHg).

Poor prognostic factor

•Pts é higher grades. •Short IP. •Cephalic tetanus. •Pts é comorbidities.

Diagnosis

Based entirely on clinical grounds. •Spatula test; touching the oropharynx é spatula ,baby develop reflex spasm of masseters, bite the spatula. •Culture from wounds for clostridium tetany or superinfection. •The CSF analysis is normal.

Treatment

Goals of Rx include; Eliminate source of toxin, Neutralize unbound toxin, Prevention of muscle spasm.

General measures

Pt should be admitted to a quiet room in ICU, where frequent monitoring is possible. If there are wounds, they should be explored & cleaned. Respiratory care includes;

Intubation & tracheostomy may be required &should be done as early as possible if indicated. These procedures are required for hypoventilation caused by laryngospasm or over sedation or to avoid aspiration. For the autonomic dysfunction; no definitive treatment has so far been outlined. But hypotension requires fluid expansion& vasopressor drug. Other measures include; hydration, nasogastric tube for nutrition. Physiotherapy should be instituted as soon as possible to avoid contracture. Input & output should be monitored. Bed sores & other infections should be prevented. Recovering pt should start active immunization for tetanus.

Specific Rx

Antibiotic: this helps to eradicate the vegetative bacteria, not the toxin. Crystalline Penicillin/Penicillin G 200.000 u/Kg/day ÷ 4 IV for 10 days for infants & children or 3 million u, IV 4 hourly for 10 days. Erythromycin & Clindamycin are alternatives for allergic pt. Metronidazole active against various anaerobic bacteria & protozoa, 15 mg/Kg/day IV or 500 mg/6 hrs or 1 gm/12 hrs (for adults).

Antiitoxin: this neutralizes only circulating toxins ẃ are not bound. Use of human tetanus immunoglobulin is the choice & should be given early. But tetanus anti-

toxin ẃ is available in our setup,can be given in doses of 10,000 u IV +10,000u IM.

Control of muscle spasm*s: Diazepam (Valium) & Chlorpromazine (Neurazien) are given 6 hourly, alternatively. Valium amp 5, 10mg, dose 0.25mg/Kg/dose IV or IM stat, suppository 5, 10 mg, then 0.1-0.2 mg/3-6 hrs IV. Fortecortine/ Dec-adrone amp 8 mg/ 2ml, 0.1 mg/Kg/dose IV/IM repeated 6 hourly, then gradual weaning. If spasms are not controlled by the above medication, neuromuscular blockers & mechanical ventilation can be used. The spasms may continue for 3-4 wks & complete recovery may take months. The neonatal mortality even é Rx is 80%, clinical tetanus does not produce state of immunity, therefore survived infant will require active immunization.

Prevention

Immunization of pregnant women é tetanus toxoid, 2 doses of tetanus toxoid to all pregnant women between 16-36 wks of gestation é interval of 1-2 months between the 2 doses, highly recommended in developing countries. If pregnant woman previously immunized, booster dose is sufficient. If pregnant woman not immunized, the NN should be protected against tetanus by giving tetanus human immunoglobulin 750 U within 6 hrs of birth.

RABIES

One of the so called “neglected zoonotic diseases”. High case fatality rate. Rabies is acute CNS disease that is caused by rabies virus.

Etiology

Rabies virus is single stranded RNA virus ẃ belongs to rhabdovirus family.

Epidemiology

Rabies is found in animals in most regions of the world. Source of infection could be domestic or wild animals. It is 100% preventable, about 55.000 humans die from it each yr around the world, mostly from exposure to dogs. Human infection occurs through contact é unimmunized domestic animals or exposure to wild animals like fox & bats. Domestic dogs are responsible for >90% of cases. The IP of rabies is very variable, ranges from 7 days to as late as 〉1 yr, (mean 1-2 mon).

Pathogenesis

Virus enters the body through skin or mucous membrane. There is initial replication of virus at the muscles around port of entry then virus ascends to the CNS through the neuromuscular junction. Once in the CNS, the virus replicates in the grey matters. The virus then passes to other organs like kidneys, salivary glands, heart & skin, following the autonomic nervous system. The passage of the virus into Salivary gland facilitates further transmission.-

Clinical manifestations

1. Prodromal stage: usually lasts 〈4 days; manifested by fever, headache,

malaise, anorexia & vomiting.

2. *Encephalitis phase:* starts é excitation & agitation, later there will be confusion, hallucination, aggressive behavior, muscle spasm, meningismus, opisthotonus, seizure & focal paralysis. Pt may have fever, irregular pupils, salivation, perspiration & postural hypotension.

***3. Brain stem dysfunction*:** begins soon after the encephalitis phase. Multiple cranial nerve deficits. Excessive salivation & inability to swallow the excessive saliva. Hydrophobia is seen in 50% of cases.

4. Death: pt rapidly develop coma, death due to respiratory failure.

Laboratory Findings

Early in the course, the routine investigations are normal. Later the WBCs usually moderately elevated, but it may as well be normal. However, diagnosis rests on identification of the virus or serologic tests, PCR of skin biopsy, serology (direct flu-orescent antibody test).

Treatment

Once clinical disease appears, mortality is 100%. Therefore any one é history of domestic or wild animal bite should be taken seriously.

Post exposure prophylaxis

Should be considered in people who had physical contact é saliva or secretions of infected animals or bitten by unprovoked animal. This include;

rigorous cleansing & Rx of the wound. Administration of Rabies Vaccine + Anti-Rabies Immunoglobulin. As the IP of rabies is variable, post exposure prophylaxis should be initiated as long as there is no clinical evidence of rabies.

Cat

SEXUALLY TRANSMITTED INFECTIONS

Diverse group of infections caused by different types of microbial agents, that are frequently transmitted by sexual contact. At present there are >20 known causes of STDs. Most STDs are rarely if ever transmitted by fomites, food, flies, or casual contact. At least one sexual partner is always infected; the apparent exceptions usually can be attributed to prolonged subclinical infection in one/both partners. So, risk assessment & management of sexual partners are important.

Epidemiology

STDs are major public health problems in all countries, but are especially in developing countries where access to adequate diagnostic & management facilities is very limited or non-existent. There is limited information on the incidence & prevalence of STDs in Egypt. Large proportion of STDs are sympto-matic & most symptomatic pts seek Rx from traditional healers, pharmacists….

URETHRAL DISCHARGE

Is the most common presenting compliant of men é STDs. In urethral discharge, exudate is present in the anterior urethra & discharge is often accompanied by dysuria or urethral discomfort. It may lead to epididymitis & complications such as infertility & urethral stricture.

Aetiology

For practical purposes, STDs-related urethritis is divided into the following:-

Gonococcal urethritis: caused by Neisseria Gonorrhoea, also known as Gonoc-occi, or Gonococcus, is a species of Gram -ve coffee bean-shaped diplococci bacteria responsible for the sexually transmitted infection “gonorrhoea”. It has IP (2-3 days). Vast majority of cases present é abundant, purulent discharge. Tend

to produce more severe UTI symptoms like dysuria, urgency & frequency.

Nongonococcal urethritis: usually caused by Chlamydia Trachomatis or Ureaplasm Urealyticum ẃ is a bacterium belonging to the family Mycoplasmataceae. Ureaplasm noted for its lack of cell wall. It is found in about 70% of sexually active humans. Its type strain is T 960, has long IP (1-3 wks). Has scanty to moderate, white, mucoid/serous discharge & mild UTI symptoms. The quantity & appearance of the discharge can be used to distinguish accurately Gonococcal from Non-Gonococcal urethritis in 75-80% of pts who have not urinated recently. It can't of course, be used to diagnose dual infection é N. Gonorrhoea & C. Trachomatis. Milking of urethra may be necessary to get good amount of discharge sample.

Laboratory

Microscopy of urethral discharge stained é methylene blue or gram stain shows: pus cells é intracellular coffee bean shaped diplococcic é gonococcal urethritis, while it shows pus cells éout intracellular diplococcic in non-gnococcal urethritis.

Treatment

When the accurate etiologic diagnosis is made include:-

Gonococcal Urethritis

Treated é Ceftriaxone 250 mg IM stat, or Ciprofloxacin 500 mg PO stat. or Spectin- omycin 2 mg IM stat.

Non Gonococcal Urethritis

Treated é Doxycycline 100 mg PO BID for 7 days or Tetracycline 500 mg PO QID for 7 days, or Erythromycin 500 mg PO QID for 7 days.

When there is no etiologic diagnosis: treatment should cover both Gonococcal & Chlamydial infections.

VAGINAL DISCHARGE

Aetiology

①Nisseriagonorrhea ②Chlamydia Trachomatis ③Trichomonas Vaginalis ④Gardnerella Vaginalis ⑤Candida Albicans ⑥Vaginal anaerobes (“bacterial vaginosis”). The first 3 are sexually acquired. The last 3 are endogenous infection. Also the first 2 cause cervicitis while the last 4 cause vaginitis. Bacterial vaginosis is the leading cause of vaginal discharge. As urethritis in males. Coinfection é Chlamydia Trachomatis is common in women é gonorrhea (~50%).

Clinical picture

Many women have a small amount of vaginal discharge (Physiologic leucorrhoea), ẃ is clear & odorless. It becomes abnormal if the woman notes a change in the amount, color or odor of the discharge. In general, most women é abnormal vaginal discharge will complain of excessive secretions, soiling of undergarments, changes in color &/or odor of discharge, may be associated ē itching, dysuria, dyspareunia & redness of vulva. Sometimes accompanied by lower abdominal pain. The initial assessment of pt who has vaginal discharge include:-

-Risk assessment.

-Clinical evaluation é speculum examination to determine site of infection.

Vaginitis

Bacterial vaginosis & vaginal trichomoniasis are more frequent among sexually active women while vaginal candidiasis occurs when there is impairment of local or systemic defensive mechanism. The discharge in bacterial vaginosis is homogenous é typical fishy odor due to the presence of volatile amines & this may be apparent during examination or when the discharge is mixed é 10% KOH.

The discharge in trichomoniasis is profuse, runny, mal odorous, while that of vaginal candidiasis is often white, curd-like é pruritus. On speculum exam of isolated vaginitis, the cervix looks healthy & discharge is not coming from the cervix.

Cervicitis

Is frequently asymptomatic. It may be detected on routine pelvic examination or during evaluation of pt é vaginal discharge. Presence of purulent exudates from the cervical os indicates infection é Neisseria Gonorrhea or Chlamydia.

Risk factors for vaginal discharge

- Multiple sexual partners in the last 3 months.
- New sexual partner in last 3 months.
- Age ˂25 yrs.
- Having ever traded sex.

Complications of vaginal discharge

- Infertility. - Chronic pelvic pain. - PRM during pregnancy. - Preterm labour.

Laboratory investigations

Specimen of vaginal discharge used mainly for the diagnosis of trichomoniasis, bacterial vaginosis & candidiasis. In trichomonos vaginalis; characteristic jerky motility of the parasite é many WBCs. In bacterial vaginosis; typical fishy odour ẃ enha- nced by the addition of 1-2 drops of potassium hydroxide to the specimen of vaginal discharge (sniff test); number of epithelial cells per microscopic field exceeds the number of leukocytes (cornified squamous epithelial cells covered by coccobacilli “Clue cells”). In candidiasis; look for yeast, the addition of 10% KOH may improve diagnostic sensitivity. **N.B.** in general, Gram stain not helpful in diagnosing gonorrhoea in females (low sensitivity).

Treatment

Trichomonos Vaginalis: Metronidazole 2 gm PO stat.

Bacterial Vaginosis; only for symptomatic women, Metronidazole 500 mg PO, BID for 7 days or 2 gm (single dose), repeat after 2 days.

Vulvovaginal Candidiasis; topical antifungal; Nystatin 100,000-1,000,000u/day intravaginally for 14 days, or Clotrimazole 200 mg intravaginally/day for 3 days.

Mucopurulent discharge; Rx for gonorrhoea & chlamydia.

Recommended treatment for Vaginal Discharge syndrome	
Risk Assessment +ve	Risk Assessment -ve
Ciprofloxacin 500mg PO stat or Spectinomycin 2gm IM stat + Doxycycline 100 mg PO BID for 7 days + Metronidazole 500 mg Po ID for 7 days	Metronidazole 500mg Po ID for 7 days + Clotrimazole vaginal tabs 200 mg at bed time for 3 days

GENITAL ULCER

Is loss of continuity of the skin of the genitalia, is either painful or painless & frequently accompanied by inguinal lymphadenopathy.

Causes

Syphilis

Caused by Treponema Pallidum. The genital ulcer occurs in the 1ry stage of the diseases. Starts as small papular lesion that rapidly ulcerates to produce a non-tender indurated lesion é clean base & raised margins known as chancre. The chancre may appear at any point of contact: genitals, anus, mouth. The ulcer heal éout treatment in 1-6 wks. Swollen LNs may appear.

Complications

- Secondary Syphilis.
- Aortitis é valvulitis.
- Neurosyphilis.

Management

Benzanthine Penicillin 2.4 million U IM stat or Procaine Penicillin 1.2 million U daily IM for 10 days. In Penicillin allergic pts, Idoxycycline 100 mg PO BID for 15 days

Genital Herpes

HSV has 2 types; HSV-1 causes dominantly oral disease & HSV-2 causes dominantly genital disease. Worldwide, herpes is the most common cause of genital ulcer. Latency & frequent recurrence characterizes genital herpes, producing a lifelong infection. Herpetic ulcers usually painful & multiple. Starts as clear vesicle & becomes pustule ẃ later erodes to an ulcer & then crusts. Heals spontaneously after 2-3 wks. Recurrence possible but milder (the number of vesicles are fewer). It tends to be aggressive in HIV pt é extensive tissue involvement & chronic ulceration. May also disseminated to CNS, or skin.

Complications: Recurrence Aseptic meningitis Encephalitis.

Management: Acyclovir (200 mg tab) 15 mg/ kg/day ÷ 3 for 10 days.

Chancroid

Caused by Haemophilus Ducreyi, is one of the commonest causes of genital ulcers. IP: 3-15 days. Ulcer on the penile shaft or prepuce. It is painful progressing from small papule to pustule, then ulcer é soft margins described as soft chancre é yellow grey exudative covering & erythema. Inguinal lymphadenopathy that becomes necrotic & fluctuant (bubo) follows the ulcer within 1-2 wks.

Complication: penile auto amputation.

Management: Ceftriaxone 250mg 1M stat or Erythromycin 500mg TID for 7 days.

Lymphogranuloma Venereum

Caused by L1, L2 & L3 serovars of Chlamydia Trachomatis. Major pathology occurs in the lymphatic system. The primary stage is marked by a painless vesiculopapular ulceration at the site of inoculation, located in the penis in men & on the labia & posterior vagina in women. The primary lesion usually not noticed. The secondary stage is described as the inguinal syndrome; a painful inguinal lymphadenitis ē constitutional symptoms. In men infection usually spreads through the lymphatics causing inguinal & femoral lymphadenitis. In women upper vaginal & cervical infection results in enlargement of the obturator & iliac LNs (sometimes pelvic LNs). Inguinal lymphadenopathy is usually unilateral (2/3 of cases). The LNs initially discreet & later becomes fluctuant & suppurative developing multiple draining fistulas. Bubo may grooved by the inguinal ligament "groove sign". External genitalia may be oedematous & swollen. May cause anatomical distortion, particularly of penis. Spontaneous healing after several months possible.

Complications: genital elephantiasis, adhesion, stricture & fistula of penis, or urethra or rectum.

Management: Doxycycline 100 mg PO BID for 14 days or Tetracycline 500 mg PO QID for 14 days

Granuloma Inguinal

Chronic & progressively destructive bacterial infection of the genital region éout systemic symptoms.

Aetiology: Calymmato bacterium Granuloma is G-ve intracellular bacteria, transmitted through sexual & nonsexual contact. Distribution mainly in Australia,

Caribbean, India, Southern Africa.

Clinical manifestation: IP usually 1-4 wks, may be as long as a year. Pt usually presents é non suppurative genital lesion ẃ develops from small firm papule to painless ulcer é beefy red appearance &non purulent base. Lesion bleeds easily & expand gradually. 50% of women have lesion on cervix & 6% have extra inguinal.

Complications:•Elephantiasis of labia •Adhesion •Urethral/vaginal/rectal stenosis.

Management: Cotrimoxazole 2 tab PO BID for 14 days.

NB: tetracycline is contraindicated during pregnancy.

INGUINAL BUBO

Inguinal bubo is enlargement of the lymph glands in the groin area.

Aetiology: the common sexually transmitted pathogen associated é Inguinal bubo include:-

Chlamydia Trachomatis server L1-L3 (Lymphogranuloma Venereum). Haemophilus Ducreyi (Chancroid). Calymmatobacterium Granulomatis (Granuloma Inguinal). Treponema Pallidum (Syphilis) may sometimes cause it. Except in case of LGV, bubo is rarely a sole manifestation of STDs & usually found together é the aetiologically related genital ulcer. Non-sexually transmitted local or systemic infections can also cause inguinal lymphadenopathy.

Clinical feature: usually pt complains of unilateral or bilateral painful swelling in the groin, but bubos can be painless.

Treatment: fluctuant buboes require aspiration through adjacent healthy skin & don't incise for drainage. If genital ulcers are present, treat é the aetiologically related cause.

Recommended Rx Inguinal Bubo Ciprofloxacin 500 mg PO BID for 3 days + Doxycycline 100 mg PO BID for 14 days or Erythromycin 500 mg PO BID for 14days

SCROTAL SWELLING

The cause of scrotal swelling depend on the age of the pt: for those ‹35 yrs: Nisseria Gonorrhoea & Chlamydia Tracomatis. For those›35 yrs: Gram -ve organisms, TB & other causes including Brucellosis, Mumps, Onchocerciasis, Wuchereria Buncrof ti. It is important to exclude other causes of scrotal swelling ẃ may require urgent surgical evaluation & management as; testicular torsion, trauma, or incarcerated inguinal hernia.

Complications: •Epididymitis •Infertility •Impotence •Prostatitis.

Management

- Supportive Rx; analgesia & scrotal support may be indicated é severe pain.
- Antibiotics; Ciprofloxacin 500 mg PO or Spectinomycin 2 gm IM stat + Doxycycline 100 mg PO BID, or Tetracycline 500 mg PO QID for 7 days.

LOWER ABDOMINAL PAIN

Lower abdominal pain in women is associated é PID e.g. salpingitis, endometritis, parametritis, oopheritis, caused by microorganisms ẃ generally ascend from lower genital tract to invade the endometrium, fallopian tubes, ovaries, other adjacent tissues & peritoneum.

Aetiology: commonly Neisseria Gonorrhoea & Chlamydia Trachomatis. PID often polymicrobial & may be associated é mycoplasma, bacteroids, strept, E. coli, H. influenza, ẃ may not be sexually transmitted.

Risk factors: The occurrence of vaginal discharge may be an antecedent event.

The risk factors include; STDs, IUDs, postpartum & postabortal ascending infections.

Clinical features: mild to severe bilateral lower abdominal pain is the most common complaint, ẃ may first to be noticed during or shortly after menses & ẃ is sometimes associated é fever. Presence of vaginal discharge support the diagnosis of PID, pain during intercourse or urination may also be present.

Physical examination: lower abdominal & adnexal tenderness together é cervical excitation may be indicative of PID. Tender pelvic mass together é fever, nausea /vomiting can also be detected. Vaginal discharge, genital ulcer, presence of IUD, open cervix (abortion tissue seen or felt) support the diagnosis of PID.

Diagnosis: is often difficult. Over diagnosis & Rx may be justified in order to prevent complications. R/O other cause of lower abdominal pain in women as appendicitis, ectopic pregnancy & cholecystitis. Direct wet mount microscopy of a vaginal specimen is necessary. The presence of pus cells in numbers exceeding those of epithelial cells suggests infection of the lower genital tract.

Complications: peritonitis -Intra-abdominal abscess -Adhesion -Intestinal obstr-uction -Ectopic pregnancy -Infertility.

Treatment: most pts. é mild/moderate PID can treated as out pt. Some pts need hospital admission. Indications for admission include; uncertain diagnosis, pelvic abscess, pregnancy, coinfection é HIV. As the infection is polymicrobial in nature instead of single, combination of antibiotics should be prescribed. The spectrum of antimicrobial should cover the following organisms; N. Gonorrhoea, C. Trachomatous, Aerobic & Anaerobic Bacteria. Antibiotics should be initiated empirically even before the microbiological report is available.

Recommended Rx for lower abdominal pain as Out patient	Recommended Rx for lower abdominal pain as In patient
Ciprofloxacin 500 mg PO stat or Spectinom-Ycin 2 gm IM stat + Doxycycline 100 mg PO BID for 14 days + Metronidazole 500mg mg PO/day for 14 days. Admit the pt if there is no improvement within 72 hrs.	Metronidazole 500 mg PO/day for 7 days + Clotrimazole vaginal tab. 200 mg at bed time for 3 day.

NEONATAL CONJUNCTIVITIS

Defined as mucoid, mucopurulent or purulent discharge from one or both eyes in the first month of life. Any discharge, even a watery secretion from baby`s eyes during the first week should be viewed é suspicion, since tears are not secreted so early in life. Neisseria gonococcal cause mucopurulent/purulent discharge, marked chemosis & retractor may be required to examine the eyes, the eye lids are tense & swollen, a false membrane may be form. Corneal ulceration may occur. It is preventable disease occurring in newborn baby due to maternal infection acquired at the time of birth & used to be responsible for 50% of blindness among children. Recently -NN conjunctivitis almost eliminated except in communities é poor hygiene & limited health care.

Differential diagnosis

Gonococcal infection, Chlamydial, other bacteria, viral, or congenitally blocked nasolacrimal duct, or dacrocystitis.

Bacteriological examination: examination of discharge, or conjunctival scrapings, should be done in every case, gram stain, culture/sensitivity.

Complications: ◎Perforation. ◎Cataract. ◎Panophthalmia. ◎Corneal opacities.

Management

According to the time of onset, classified as follow:-

❁Seen within the first 48 hrs of life: Neisseria Gonorrhoea-treated é Ceftriaxone IM, Gentamicin drops, Bacitracin ointment. Chemical conjunctivitis needs washing of eyes, Erythromycin ointment, observe, usually improves in 24 hrs.

❁Seen within the 48-72 hrs of life: Staph, Strept, G-ve Coliforms, treated é Neom-ycin/Bacitracin ointment. Gentamicin or Tobramycin drops.

❁Seen within the 5^{th}-7^{th} day of life: HSV-II, treated é Acyclovir 3% eye ointment, systemic Acyclovir for systemic involvement.

❁Seen after the 1^{st} wk of life: Chlamydia Trachomties, treated é Erythromycin/ Chlortetracycline eye ointment. Oral Erythromycin for systemic infection & pare-nts to be treated.

Differential Diagnosis of Bacterial, Viral & Allergic Conjunctivitis

Clinical Finding	Bacterial	Viral	Allergic
Bilateral eyes	50% to 74%	35%	Mostly
Discharge	Mucopurulent in younger children	Mild, watery, or "sleepers" only	Rare
Redness	Common in older children, uncommon in infants and toddlers	Usually	Usually
Acute otitis media	32% to 39%	10%	No
Pruritic	No (but many rub eyes)	No	Major

TYPHOID FEVER

Definition

Systemic infection characterized by fever & abdominal pain, caused by dissemination of salmonella typhi & occasionally salmonella paratyphi A, B & salmonella typhimarium. All of them are non-capsulated, G -ve motile bacteria.

Epidemiology

Human beings are the only hosts for salmonella typhi & paratyphi, thus enteric fever is transmitted only through close contact é acutely infected individual or chronic carrier through ingestion of contaminated food or water. Chronic carriers are the source of infection harbouring the organisms in their gall bladder (especially in presence of gall stones) & rarely at other sites. It affects people of all ages & both sexes. Typhoid is endemic in most developing countries. The disease observed at great frequency in AIDS pts than general population.

Pathogenesis

Following ingestion of the organism in contaminated food/drink, salmonella typhi passes the gastric barrier & reach the upper small intestine where the bacilli invade the intestinal epithelium &they are engulfed by phagosoms ẃ reside in the payer's patches. The bacilli multiply & enter the blood stream causing transient bacteraemia. At this stage salmonellae disseminate throughout the body in the macrophages via lymphatic & colonize RES (liver, spleen, LNs & bone marrow). Pts have relatively fewer or no signs & symptoms during this initial IP. The signs & symptoms, including fever & abdominal pain result when a critical number of bacteria have replicated during wks after initial colonization, further inflammation of Payer's patches may result enlargement & necrosis ẃ may result

in intestinal Hge & perforation. Infection may become persistent & invade gall bladder. The clinical phase of typhoid fever depends on host defense & bacteria multiplication.

Clinical manifestation

IP varies from 3-60 days & manifestation is dependent on inoculum size, state of host defence & duration of the disease. Severity of the illness range from mild, brief illness or acute severe disease or CNS involvement & death.

1st wk: fever is high grade é daily ⇧ in a stepladder pattern for the 1st wk then becomes persistent. Headache, malaise & abdominal pain. Initially diarrhoea followed by constipation in adults, while diarrhea is dominate feature in children. Relative bradycardia. Splenomegaly & hepatomegaly. Rose spots not commonly seen in black pts. In whites it appears as small, pale red, blanching macules commonly over chest, abdomen & back lasting for 2-3 days. Epistaxis may be seen.

2nd wk: fever becomes continuous. Pt becomes very ill, withdrawn, confused, delirious & sometimes may be even comatose.

3rd wk: pt goes to a pattern of “typhoidal state" characterized by extreme toxa-emia, disorientation, “pea-soup” diarrhea & sometimes may be complicated by intestinal perforation & Hge.

4th wk: fever starts to decline**,** pt may defervesce é resolution of symptoms. At this point pt may lose weight. Relapse may occur in 10% of cases.

Rose spots on 5th day on the trunk.

Complications

GIT perforation & Hge are late complications that may occur in the 3rd - 4th wk. May develop despite clinical improvement. These complications are life threatening & need immediate medical & surgical interventions. Other less common complications include; hepatitis, meningitis, arthritis, osteomyelitis, parotitis, orchitis, nephritis, myocarditis, bronchitis & pneumonia. These complications can be prevented by prompt diagnosis & Rx of typhoid from the start.

Chronic carriers

1-5% of pts become asymptomatic chronic carriers. They shed salmonella typhi in either urine or stool for >1 yr. The incidence is higher in women & among pts é biliary abnormality (stone or carcinoma of gall bladder) & other GIT malignancies.

Diagnosis

Suggested by the presence of:-

- Persistent fever.
- Relative bradycardia found to occur in 80% of cases.
- Rose spots seen in 70% of whites & 20% of others.
- Leukopenia.

But definitive diagnosis of the disease requires laboratory tests including:-

- **Blood culture:** up to 90% of pts have +ve culture in the first week & only 50% by the third week. The yield is much lower if pt has taken antibiotics prior to the test
- **Stool culture:** is -ve in the first wk, becomes +ve in 75% of pts in the third wk. Urine culture parallels stool culture.
- **Widal test for O & H antigens:** the O (somatic) antigen indicate active infection, whereas the H (flagellar) antigen could be indicative of past infection or immuniz-

ation of typhoid. Widal test is a test involving agglutination of typhoid bacilli when they are mixed é serum containing typhoid antibodies from an individual having typhoid fever; used to detect the presence of salmonella typhi & para-typhi. The widal test has certain limitations & to make a diagnosis of current infection a 4 X (fold) ⇧ in titer on paired sera taken during the acute & convalescence phases is necessary (in normal individual widal test value is < 160).

Limitations of Widal test: include the following; it is non specific & +ve test could be due to; •Infection by other salmonellae (as the antigen used for the test is also shared by other salmonellae). •Recent vaccination for typhoid, or •Past typhoid infection (already treated). The demonstration of 4 -fold ⇧ in titer on paired sera is not useful for Rx of acute cases, as this requires waiting for the convalescence phase & at this stage if the pt is lucky recovery will occur.

o**PCR for typhoid.** in general the PCR is the most sensitive of the existing rapid methods to detect microbial pathogens in clinical specimens.

Treatment

Antibiotic Rx is curative. These drugs can be given either PO or IV, depending on pt condition & the severity of the disease. One should note that fever may persist for 4-6 days despite effective antibiotic Rx. First line nowadays for Rx is 4-Amino Quinolones ẃ are the drugs of choice because of their effectiveness on multidrug resistant typhoid, low relapse &carrier rates. Ciprofloxacin, Norfloxacin ,Ofloxacin are all equally effective. Other antibiotics as ampicillin, chloramphenicol, trimethoprim-sulfamethoxazole, amoxicillin are also effective.

Claforan (cefotaxime) 500 mg amp, 50 mg/kg/D÷3 IV, OR Oral 4th generation cephalosporin as; Orelox sy 40,100 mg, 8 mg/Kg/D ÷2 X 5D, or Zinnat sy, 125mg, 8mg

/Kg/D ÷2 X 5D. IV Drugs recommended for critical pts or for pt unable to take orally.

Prompt administration of high-dose dexamethasone reduces mortality in pts ē severe typhoid fever without increasing incidence of complications, carrier states, or relapse among survivors. Initial dose of 3mg/kg by slow IV over 30 min, 1mg /kg 6 hourly for 2 days.

Chronic carrier eradication

-Ciprofloxacin for 4 wks is effective, much better than other drugs. or

-Ampicillin or Amoxicillin 100 mg/kg/D taken é Probencid 30mg/kg/day for 6 wks

-Cotrimexazole (160/800 mg twice a day) + Rifampicin 600 mg PO/ day for 6 wks.

N.B. drug treatment does not eradicate infection in 40% of cases of chronic carriers. Hence surgical resection of gall bladder may sometimes be necessary.

Prevention & control of typhoid

✶Improve environmental sanitation.

✶Identification& Rx of chronic carriers.

✶Avoid food handling by chronic carriers.

✶Vaccination for food dealers, those working in restaurants, vaccination of travellers to endemic areas: - live oral vaccine 3 dosses can be given to those **>** 6 yrs, is protective for several yrs. The purified Vi polysaccharide vaccine given in a single dose to those **>**2 yrs age & HIV +ve individuals, is as effective as live vaccine.

BRUCELLOSIS

Zoonotic disease caused by Brucella species characterized by remittent type of fever & multiorgan involvement. Is transmitted to humans from infected animals.

Aetiology: it is caused by 4 different types of Brucella. They are small aerobic Gram -ve bacilli; are non-motile & facultative intracellular, include:-

Brucella melitensis (the most common & most virulent type) acquired from goats ,sheep & camels. **Brucella abortus** from cattle. **Brucella suis** from hogs. **Brucela canis** from dogs.

Epidemiology: it is found worldwide, but the true incidence is not known. In communities where brucellosis is endemic, it occurs in children & family members of infected persons are at risk. Commonly affected are farmers, meat-processing workers, veterinarians & lab workers. Brucella is transmitted commonly through the ingestion of untreated milk/or milk products, raw meat & bone marrow have been implicated. But also transmitted by inhalation from close contact é animals.

Pathogenesis: in blood, brucella ingested by PMNLs & macrophages but they resist intracellular phagocytosis. Severity of the disease is largely determined by the outcome of pathogen-phagocyte interaction. The organisms multiply, reach blood stream via lymphatics & then reside in different organs; liver, spleen, bone, kidneys, LNs, heart valves, nervous system & testes. In the infected organs there

will be inflammatory responses or non-caseating granulomas. Serum IgM will appear within a wk & later on IgG & IgA.

Clinical manifestations & complications

Brucellosis is a systemic illness & its manifestations mimic other febrile illnesses. The IP is about 1-3 wks. The illness may begin suddenly or it could be gradual. The most common symptoms are fever, chills, sweating especially by night, headache, myalgia, fatigue, anorexia, joint or low back pain, Wt loss, generalised lymphadenopathy, constipation, sore throat & dry cough. Pt may look well é no findings or may exhibit physical findings related to the organ affected. Fever has no distinctive features but it occurs in late afternoons or evenings. Pts may have reactive asymmetric polyarthritis involving the large joints & lumbar vertebral osteomyelitis. CVS complications of brucellosis include endocarditis, myocarditis, pericarditis, thrombophlebitis &pulmonary embolism. Respiratory manifestations like sore throat, tonsillitis, dry cough, even pneumonia &lung abscess. The GIT manifestations are generally mild include; nausea, vomiting, abdominal pain & diarrhea; there is tender hepatosplenomegaly (Morphy sign) in about 15-20% of pts. Pts may have genitourinary infection &present é epididymoorchitis, prostatitis, amenorrhea, tub ovarian abscess, salpingitis, acute pyelonephritis & glomerulonephritis. The Nervous system involvement is uncommon but if involved, pt may have meningitis, brain abscess, hemiplegia & cranial nerve deficit. Other manifestations are conjunctivitis, retinopathy, abortion, anemia, leukopenia & thrombocytopenia.

Diagnosis:

- History of exposure & Clinical features.

•Significantly ⇧ levels of Brucella agglutinin >1/160 confirms the active infection.

•CBC: leukopenia é lymphocytosis.

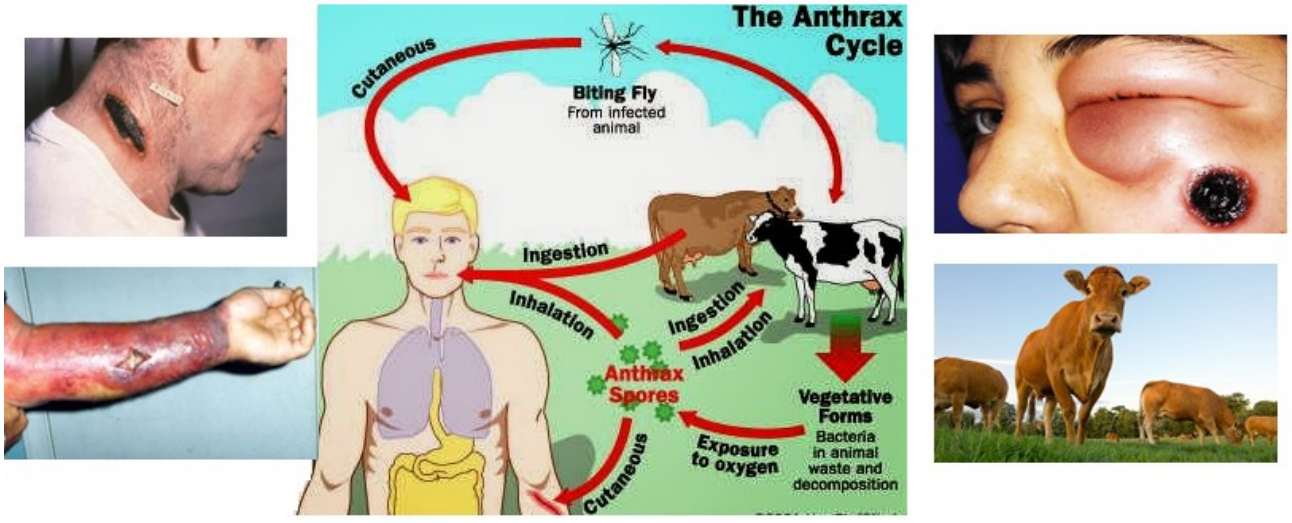
•Blood C/S. •Antibodies for brucella (IgM) •ELISA •PCR.

Treatment

The combination of Doxycycline & Aminoglycoside for 4 wks followed by the combination of Doxycycline & Rifampin for 4-8 wks is the most effective Rx. Pt é serious illness & complication need admission for Rx é IV medications & possible surgical intervention.

Prevention: immunization of animals, boiling or pasteurizing milk.

ANTHRAX



Is occupational disease, affect workers in farms & dealer é animals. The disease transmitted from infected animals to man through skin to skin contact, causing an ugly ulcer, or through inhalation of spores from dead animal tissue causing respiratory symptoms, pneumonia, or through ingestion of spores in undercooked meat causing GIT symptoms & may lead to meningitis.

Aetiology: Bacillus anthracis is a large, aerobic, spore-forming, G +ve rod, ẃ is en-capsulated & non-motile.

Epidemiology: is more common in herbivorous animals like cattle, sheep& goats. They are infected while grazing on contaminated grass. Humans may acquire anthrax from agricultural sites through contact é animal like butchering & feeding or from industrial sites thr-ough exposure to contaminated hides, wool or bones.

Pathogenesis: cutaneous anthrax is initiated when spores of *B.* Anthracis are intr-oduced through abrasions of the skin or insect bite. Inhalation anthrax is acquired by directly inhaling the agent. The GIT form is acquired through ingestion of cont-aminated raw or partially cooked meat. Bacillus Anthracis goes to the blood stre-eam & replicates rapidly. It is resistant to phagocytosis & produces anthrax toxin, ẃ cause oedema & inhibition of polymorph nuclear leucocyte function. Moreover it causes release of cytokines, shock & death.

Clinical Manifestations: IP is 1-5 days. About 95% of anthrax is cutaneous form, 5% is through inhalation. The GIT form is very rare & is more common in areas where raw meat is ingested.

Cutaneous Anthrax: lesions more common on exposed areas as extremities, face & neck. Lesion start as a small red macule develops within days, this will become pustule, then forms a central necrotic ulcer (black eshcar) é surrounding oedema; its painless. Usually there is associated painful regional lymphadenopathy. Most pts recover spontaneously but about 10% develop progressive infection, bactera-emia, high grade fever & rapid death.

Inhalational Anthrax (wool sorter's disease): resembles severe viral respiratory disease & thus the diagnosis is difficult. This form may be used as biological war-fare. Within 3 days of infection pt will develop fever, dyspnea, stridor, hypoxe-mia, hypotension & may die within 24 hrs once pt become symptomatic.

GIT Anthrax: Pt may have nausea, vomiting, abdominal pain, bloody diarrhea, fever & they may develop ascites.

Investigations: • CBC. • Blood culture. • Chest X ray. • Sputum culture.

Treatment

Cutaneous Anthrax: treated é Crystalline Penicillin 2 million units 6 hourly until oedema subsides then oral Penicillin for 7-10 days.

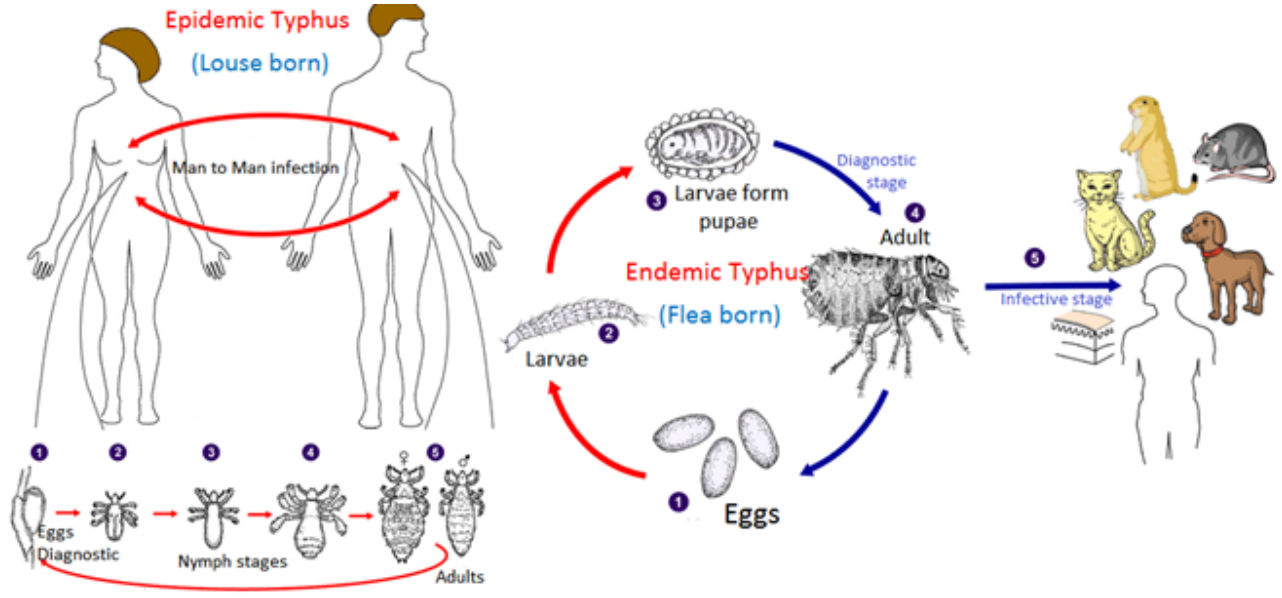
For allergic pt Ciprofloxacin, Erythromycin, or Chloramphenicol may be given. The wound should be cleaned, debrided & dressed.

Inhalation & GIT form: should treated é high dose Penicillin 8-12 million units/day ÷ 4-6 doses for 2 wks.

Mortality rate: cutaneous anthrax is 10-20%, inhalational anthrax 100% & GIT anthrax is 50%.

Prevention: • Mass vaccination of animals. • Avoiding feeding of infected cattle. • Proper disposal of dead animals & Keeping personal hygiene.

TYPHUS



Rickettsial disease. Rickettsia are small intracellular bacteria that are spread to

man by arthropod vectors, namely human body lice, fleas, ticks & larval mites by the direct bite of the vector or inoculation of the organism contained in the faeces of the vector by bite induced body itching. These infections are characterized by persistence in the body, widespread vasculitis (invading endothelial cells of small blood vessels) & multi-system involvement.

Epidemic Typhus

Louse born, caused by R. Prowazekii, transmitted by human body louse (pediculus humanus corporis). Lice acquire the rickettsia while ingesting a blood meal from an infected pt, the rickettsia multiply in the midgut epithelial cells of the louse & excr-eted via louse faeces. The infected louse defecates during a blood meal, the pt autoinoculates the organisms by scratching. The disease commonly associated é poverty, cold weather, natural disasters & wars.

Pathophysiology

In human rickettsia multiply in the endothelial cells of capillaries causing lesions in the skin, brain, lung, heart, kidneys & skeletal muscles. Endothelial proliferation coupled é perivascular reaction causes thrombosis & small hemorrhages. However, tissue & organ injury is commonly due to ⇧ vascular permeability é resulting oedema, hypovolemia & organ ischemia. This leads to multisystem involvement é complications as non-cardiogenic pulmonary oedema, cardiac arrhythmia, encephalitis, renal or hepatic failure & bleeding.

Clinical Features

•IP of epidemic typhus is one wk. •Abrupt onset of illness é prostration •Severe headache. •Rapidly rising fever of 39-40°C. •Cough seen in 70% of pts. •Myalgia may also occur ẃ may be severe. •Rash, begins on upper trunk around 5th day &

then becomes generalized, involving entire body except face, palms & soles; at first, rash is macular, becoming maculopapular, petechial & confluent éout Rx, although in black people, rash may be absent (*spotless epidemic typhus*) •Photophobia é conjunctival injetion & eye pain. •Tongue may be dry, brown, furred. •Signs of CNS involvement, commonly as meningoencephalitis, appear towards the end of first wk progressing to seizure & coma.

Brill-Zinsser disease

This is a mild form of epidemic typhus caused by reactivation of dormant R. prowazekii in the body (in LNs) as a result of immuosuppression or old age. Occurs after several yrs of acute infection. The manifestation are similar to acute epidemic typhus but milder. Organisms may infect other people in the presence of the vectors.

Endemic Typhus

Flea born, caused by R. typhi. Fleas acquire R. typhi from rikettsemic rats, carry the organism throughout the rest of their life. Humans & Rats are infected when rickettsia laden fleas are scratched into pruritic bite lesions. Endemic typhus is relatively milder, its IP is 1-3 wks, followed by sudden onset of fever, rigors, frontal headache, pain in the back & limbs, constipation & cough. Fever becomes constant after the 3rd day, associated é conjunctivitis & orbital pain. Rash appears on the 5th day initially as blanching macules at the anterior axillary folds, ẃ subsequently spread to involve other parts of the body (sparing face & neck) & become purpuric. During the 2nd wk symptoms worsen & additional manifestations, as sore lips, dry brown tremulous tongue, feeble pulse, enlarged spleen & delirium.

Complications

•Skin necrosis, gangrene of digits •Venous thrombosis •Interstitial pneumonia in severe cases •Myocarditis •Renal failure •Parotitis.

Diagnosis

•Based on history, clinical course & epidemiologic of the disease.

•Indirect fluorescent antibody test.

•Weil-Felix agglutination test: not specific or sensitive.

•Isolation of the organism by inoculation into laboratory animals is possible, it is time consuming & technically demanding.

Treatment

Epidemic typhus

Doxycycline 200 mg as single dose PO until the pt is afebrile for 24 hour + Delousing louse borne typhus, improving hygienic condition, health education & environmental sanitation.

Endemic Typhus

Doxycycline 1500 mg bid PO for 7-15 days or Chloramphenicol 1500 mg QID PO for 7-15 days + fleas control & the prophylactic measures.

Supportive Rx: attention to fluid balance, prevention of bed sores. Treat agitation é Diazepam. Steroid (Prednisolone 20 mg/day for adults) in severe cases.

Prognosis

Untreated disease is fatal in 7-40% of cases, depending on condition of host. In untreated survivors, renal insufficiency, multiorgan involvement & neurologic manifestations (12%). in endemic typhus the prognosis is better é mortality of 1%

Prevention

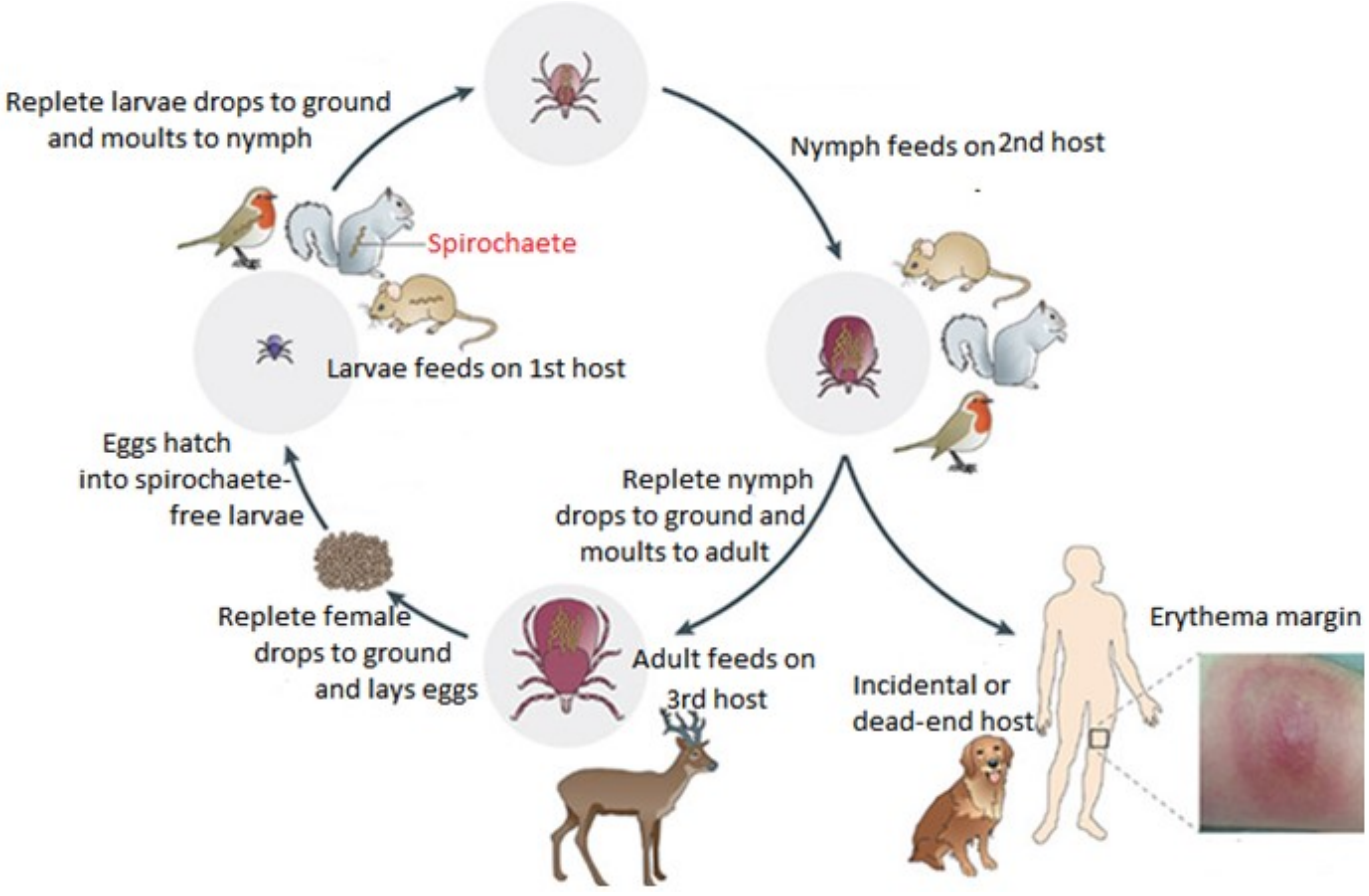
Epidemic typhus: eradicate all lice on clothing & bedding using insecticides (1% malathion powder), including all family contacts. DDT is not useful as the lice are often resistant to it. Wash the pt é soap & water & apply insecticides all over & disinfect clothing é insecticides in a bag or autoclaving. Protective wearing smeared é insect repellents is recommended for nurses & other attendants.

Endemic typhus: elimination of fleas on clothing & bedding using insecticides like 1% Malathion powder. Apply residual insecticide powder on the floor & bedding to kill hatching fleas, in addition to rodent control using chemicals.

Chemoprophylaxis

Doxycycline 100mg weekly will protect those at risk.

RELAPSING FEVER



Acute febrile illness caused by Borrelia species, presenting é recurrence of characteristic febrile periods lasting for days alternating é afebrile periods. Relapsing fever describes 2 distinct diseases:-

- Louse borne (endemic): transmitted by body louse pediculus humanis by spirochetal G -ve Borrelia Recurrentis.
- Tick borne (epidemic): transmitted by tick by spirochete Borrelia Duttoni.

Transmission

LBRF: body lice become infected by B. recurrentis while feeding on spirochetemic human blood (the only reservoir of infection). Humans acquire infection when infected body lice are crushed & their fluids contaminate mucous membrane or breaks in the skin (such as abrasions caused by scratching of pruritic louse bites). Disease affects mostly homeless men living crowded together in very unhygienic circumstances especially during rainy seasons. Some of the risk factors are overcrowding like in military camps, civilian population disrupted by war & other disasters.

TBRF: rodents are the primary hosts, the vector ticks become infected when they feeds spirochetemic rodents. Ticks transmit borrelia vertically over several generations. Is most highly endemic in subsaharan Africa but also is found in Mediterranean & Eastern countries.

Pathophysiology

In humans, borrelia after entering the body multiply in the blood & circulate in great number during febrile periods. They are also found in the spleen, liver, CNS, bone marrow & may be sequestered in these organs during periods of remission. Severity is related to spirochaetal density in blood but systemic manifestations

are related to release of various cytokines. The disease characterized by sub capsular & parenchymal Hge é infarcts of spleen, liver, heart & brain is seen. Thus , pts will have enlarged spleen & liver é variable oedema & swelling of brain, lung & kidneys. Relapsing fever in pregnancy can result abortion, or still birth & fatal NN infection. Death from TBRF is rare. In contrast fatality rate of LBRF may reach up to 20% during outbreaks, mainly among malnourished & stressed population

Clinical Features

The manifestation of both LBRF & TBRF are similar. The IP is 7 days (ranging 2-18 days). The onset is sudden é high grade irregular fever, headache, chills, myalgias, arthralgias & insomnia. Pt will be withdrawn, disinterested to food & other stimuli & thirsty. Delirium associated é high fever, tachycardia & dry tongue, injected conjunctiva & photophobia. Gallop, occasionally resulting from myocardial involvement. Upper abdominal tenderness é hepatosplenomegaly. Scattered petechiae over the trunk, extremities & mucous membrane in 1/3 of cases of LBRF & fewer TBRF. Symptoms & Signs of meningeal irritation may seen in some pts. Icteric sclera may be found in late stage of the disease. Without Rx, symptoms intensify over 2-7 days period & subside é spontaneous crisis during ẃ borrelia disappear from circulation. Such cycles of febrile periods alternating é afebrile periods may recur.

Diagnosis

•Giemsa or wright stained peripheral blood smear is the most commonly done laboratory test & the ideal test in resource limited setting. Spiral organisms can be demonstrated on peripheral blood taken during febrile period preceding the crisis, is +ve in > 70% of cases of LBRF & in lower % of pts é TBRF.

•Dark field microscopy of unstained blood/CSF •Serologic tests for Borrelia.

Complications

Life threatening complications are unusual in otherwise healthy persons if the disease is diagnosed & treated early. Complications are common in late disease in untreated pts. Complications include:-

•Epistaxis of blood streaked sputum, other bleeding tendencies.

•Neurologic manifestations like meningitis, coma, isolated cranial nerve palsies.

•Pneumonitis. •Myocarditis. •Splenic rupture.

Treatment

Antibiotics. In LBRF single dose of either Erythromycin, Tetracycline, Doxycycline or Chloramphenicol, produces rapid clearance of borrelia from the blood & remission of symptoms. TBRF is less sensitive to these antibiotics & requires a 7 days course. Doses as follow; Erythromycin 500mg/6 hrs or Tetracycline 500mg/6 hrs or Doxycycline 100 mg/12 hrs. Chloramphenicol 500mg/6 hrs. Parenteral: Penicillin (Procaine) 600,000 I.M stat & 600,000 IM daily.

Delousing of pts: important to prevent transmission/recurrence.

Jarisch- Herxheimer reaction: rapidly acting antibiotics ppt JHR within 1-4 hrs of the first dose. It is more sever in pts é LBRF than TBRF. More sever when high numbers of spirochetes circulating in blood. JHR has 3 phases:-

Chill phase: lasts for 10-30 min, rigor, hyperventilation, ⇧ COP, high fever (40^0C) accompanied by, agitation, confusion.

Flush phase: ⇩ in body temp, sweating, potential dangerous fall in BP (as peripheral vascular resistance falls), clinical & ECG evidence of myocarditis may be seen, S3 gallop & prolonged QT interval. Vitals signs must monitored closely during this

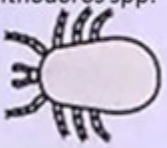
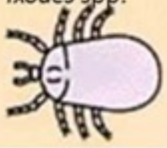
time ẃ usually lasts for < 8 hrs.

Recovery phase: vital signs slowly improve & pt is exhausted.

Treatment of JHR: close monitoring of vital signs. Careful fluid management. Control of high body temperature. Short term Digoxin IV in pts é evidence of myocardial dysfunction.

Prevention & Control

- Avoiding overcrowding.
- Applying hygienic practices & health education.
- Elimination of ticks.
- Early detection & Rx of infected persons & close contacts.
- In outbreaks of LBRF, empirical single dose Rx (Doxycycline).
- Eradication of rodents to control TBRF (Rodenticides).

	Infection	Reservoir	Vector
1. Borrelia recurrentis	Relapsing fever Epidemic (louse-borne)	Humans	Body louse *Pediculus humanus* 
2. Borrelia spp.	Relapsing fever Endemic (tick-borne)	Rodents, soft-shelled ticks	Soft-shelled tick *Ornithodoros* spp. 
3. Borrelia burgdorferi	Lyme disease	Rodents, deer, domestic pets, hard-shelled ticks	Hard-shelled tick *Ixodes* spp. 

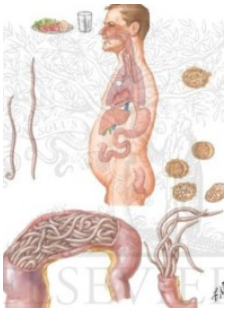
HELMENTHIASIS & PARASITIC DISEASES

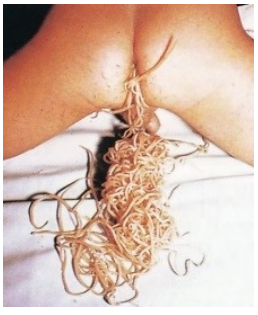
INTESTINAL NEMATODES

Nematodes

Are elongated, symmetric round worms. These can be classified as intestinal & tissue nematodes. Some of the intestinal nematode species are*, Ascaris lumbr-icoides, Necator Americanos & Ancylostoma duodenale, Strongyloides stercoralis, Enterobius vermicular is, Trichuris trichuira*more. More than a billion people wor-ld-wide are infected é one or more species of intestinal nematodes. They are most common in regions é poor sanitation, especially in developing countries. The tissue nematodes include Trichinosis, Visceral/Ocular/Cutaneous larva migr-ans, Cerebral angiostrogliasis & Gnathostomiasis.

ASCARIASIS





Ascaris Lumbricoides is the largest of the intestinal nematodes parasitizing humans & is the most common worm found in human. It is worldwide in distr-ibution & most prevalent throughout the tropics, subtropics & more prevalent in the countryside than in the city.

Morphology

Adult warm It is elongated, cylindrical & tapering at both ends. Sexes are separa-te. The female is 20-35 cm long, 4-6 mm in diameter. Male is smaller being 15-30cm long, 2-4mm in diameter. The posterior end of male is curved having penial

setae near end As many as 500-5000 adult worms may inhabit a single host.

Life cycle

The infective stage is the embryonated eggs &the route of infection is through ingestion of embryonated eggs in contaminated food or drink or from cont- aminated fingers. No intermediate & reservoir hosts. The life span of the adult is about 1 yr. Warm lives in small intestine, feeding on its contents, the fertilized female can produce approximately 240,000 eggs/day, ẃ are passed in feces (unsegmented eggs & non infective stage), they require about 3 wks in the outside environment to develop into the embryonated eggs (infective stage), after ingestion of embryonated eggs in contaminated food or drink or from contaminated fingers, host digestive juices acts on the egg shell & liberate the larva into the small intestine. These larvae penetrate the intestinal mucosa & enter lymphatics & mesenteric vessels, carried by circulation to the liver, right heart & finally to the lungs where they penetrate the capillaries into the alveoli in ẃ they molt twice & stay for 10-14 days & then carried or migrate, up the bronchioles, bronchi & trachea to the epiglottis. When swallowed, the larvae pass down into small intestine where they develop into adults. The time from the ingestion of embryonated eggs to oviposition by the females is about 60-75 days.

Pathogenesis

There are two phase in ascariasis:-

The blood-lung migration phase of the larvae: during ẃ the larvae may cause a pneumonia (low fever, cough, blood-tinged sputum, asthma) & large numbers of worms may give rise to allergic sympt- oms. Eosinophilia is generally present. These clinical manifestation is also called “Loffler’s syndrome”.

The intestinal phase of the adults warm: the presence of a few adult worms in the lumen of the small intestine usually produces no symptoms, but may give rise to vague abdominal pain or intermittent colic especially in children. A heavy worm burden can result in malnutrition. More serious manifestations have been observed. Wandering adult warms may block the appendicular lumen or common bile duct & even perforate the intestinal wall. Thus complications of ascariasis, as intestinal obstruction, appendicitis, biliary ascariasis, perforation of the intestine, cholecystitis, pancreatitis & peritonitis may occur, of ẃ biliary ascariasis is the most common complication.

Clinical Features

During the lung phase pt may develop an irritating non-productive cough & burning substantial discomfort. Fever is usual during this phase & CXR may show evidence of pneumonitis (Leoffler's sy). In established infections, pts are often asymptomatic, or may have abdominal discomfort & nausea in mild cases. In heavy infections, particularly in children, large bolus of worms may cause pain & small-bowel obstruction, or they could have chronic abdominal discomfort & growth retardation. Large worm can enter & occlude the biliary tree, causing biliary colic, cholecystitis & pancreatitis. Fatality may occur when mass of warms blocks the intestine.

Diagnosis

The symptoms & signs are for reference only. The confirmative diagnosis depends on the recovery & identification of worm or the characteristic ascaris eggs in faeces. Ascaris pneumonitis confirmed through examination of sputum for ascaris larvae is sometimes successful. For intestinal ascariasis, feces are examined for

the ascaris eggs. Direct fecal film is simple & effective. Eggs are easily found using this way due to a large number of the female oviposition, 240,000 eggs per worm/day, or recovery of adult worms: in feces or vomit.

Treatment

•Mebendazole 100 mg twice daily for 3 days or •Albendazole in a single dose of 400mg is also effective.

NB: Mebendazole & Albendazole are contraindicated in pregnancy; but Piperazine & Pyrantel pamoate & are safe.

•Piperazine 75 mg/kg (maxim 3.5 gm) single dose daily for 2 days or

•Pyrantel Pamoate in a single dose of 10 mg/kg.

Prevention

•Keeping good sanitation conditions is the only way for prevention of ascaris.

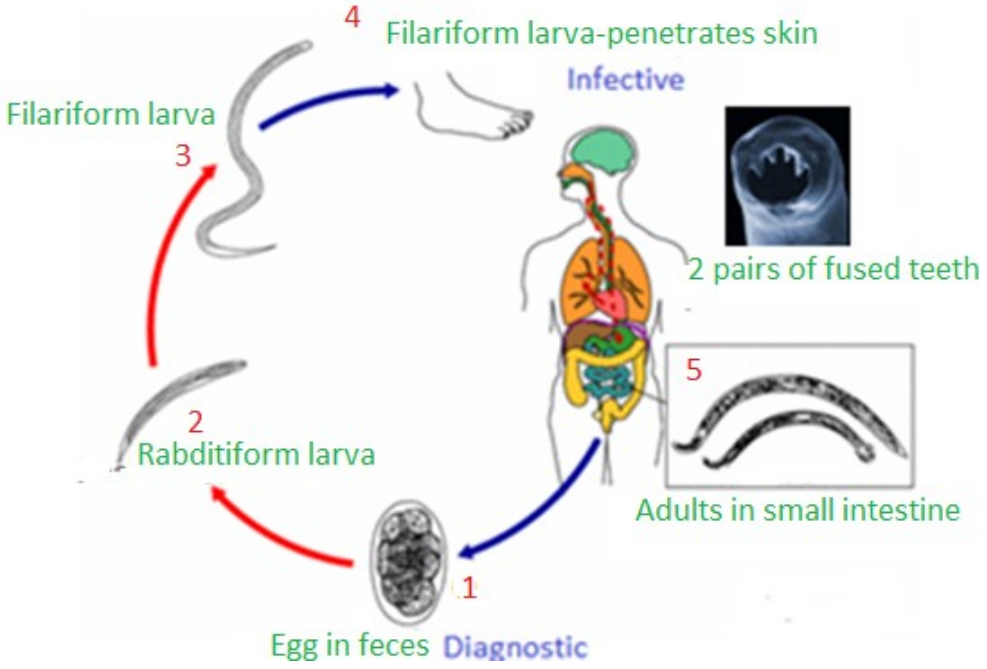
•Sanitary disposal of feces & health education.

•Pollution of soil é human feces should be avoided.

•Vegetable should be thoroughly washed in mild solution of potassium permanganate &properly cooked before use.

•Finger nails should be regularly cut to avoid the collection of dirt & eggs below them, hands should be properly washed before touching edibles or eating.

ANKYLOSTOMIASIS



2 *Hookworm* species; *Ankylostoma Duodenale & Necator Americanos.*

Epidemiology

Worldwide prevalent. But older children have the greatest incidence & intensity of hookworm infection. Prevalent in areas é poor sanitary conditions, particularly in relation to human waste disposal. Adults usually infected when walking bare-footed. Hookworm is one of the most common contributing factors for the development of iron deficiency anaemia in developing countries.

Life cycle

Adult warms are pink or creamy white. The oval buccal capsule contains 2 pairs of fused teeth. Male 8-11 mm long & female 10-13 mm. The adult hookworms live attached to the mucosa of the small intestine. Females liberate eggs into the lumen, ẃ are eliminated é the faeces. Under optimum conditions of moisture & temperature they hatch within 24-48 hrs & then develop to become infective (filariform) larvae ẃ when come into contact é unprotected human skin (usually

bare foot), they penetrate the skin layers, enter the blood stream & are transported to the lungs. Then migrate up to the bronchi, trachea & down to the oesophagus to reach small intestine where maturity is attained.

Clinical features

Most hookworm infections are asymptomatic. Infective larvae may provoke pruritic skin lesion at the site of penetration, as well as at subcutaneous migration. Infected people may rarely present é mild transient pneumonitis. In the early intestinal phase, there may be epigastric pain, inflammatory diarrhea or other GI symptoms. The major consequence of chronic hookworm infection is iron deficiency because worms suck blood from intestine. Anaemia usually develops if there is pre-existing iron deficiency states like malnutrition & pregnancy.

Diagnosis

The detection of the characteristic oval hookworm eggs in **faeces**. Eggs of the 2 species are not distinguishable. Anaemia of blood loss é hypochromic microcytic picture may be seen in **CBC.**

Treatment

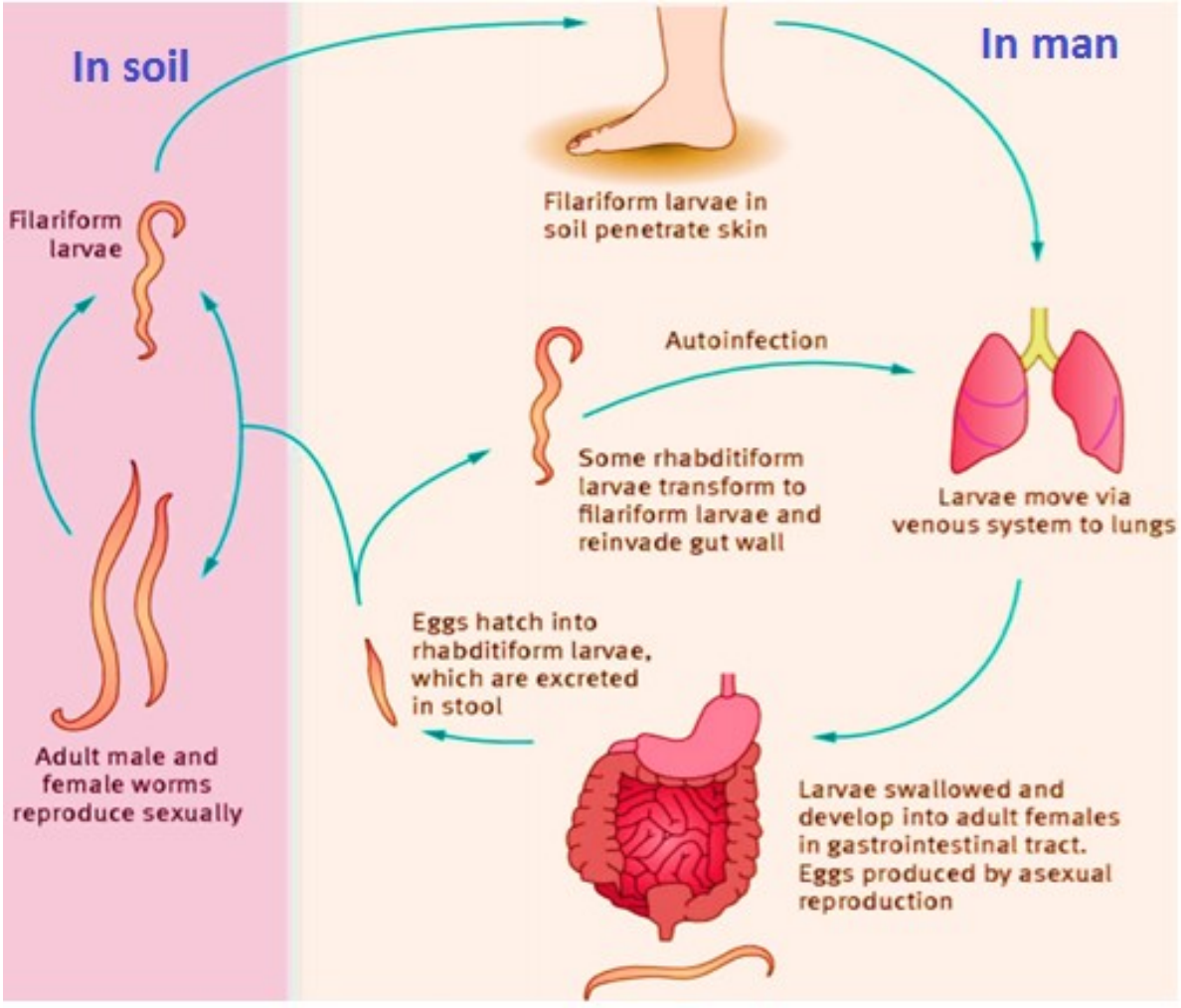
Mebendazole 100 mg twice daily for 3 days. or

Albendazole 400 mg (single dose).

STRONGYLOIDOSIS

Infection by the nematode Strongyloides Stercoralis, the female of ẃ usually is embedded in the mucosa of the small intestine of humans. Mainly distributed in tropical areas.

Life cycle



Female worm 2.5 mm long, move through the lining of the small intestine (duode num & jejunum), produce eggs ẃ laid in the mucosa of intestines, hatch within ho urs into rhabditiform larva that penetrate the glandular epithelium & pass into the lumen of the intestine & out the feces. Rhabditiform larvae can survive for some time as free-living nematodes, even reproducing through several generati- ons. Sooner or later, however infective parasitic larvae develop filariform larvae

pass in stool, it is about ½ mm long, penetrate bare skin of human (the definitive host are human, dogs & cats), move via venous system to lungs, swallowed & arriving to the intestine within a couple of days to continue their parasitic life cycle. All parasitic larva mature to female worms & reproduce éout the contribution of a male (there are males 0.7 mm in length in the free-living soil stages), the adult female worm reproduce by themselves autoinfection cycle.

Clinical features

Mild infections are usually asymptomatic. Recurrent urticaria, often involving the buttocks & wrists, is the most common cutaneous manifestation. Adult parasites burrow into the duodenojejunal mucosa & can cause abdominal pain (usually mid epigastric) ẃ resembles peptic ulcer pain, nausea, diarrhea, GI bleeding, mild colitis & wt. loss can occur. The autoinfection cycle of strongyloidosis is normally contained by unknown factors of the host's immune system. In immunocompro-mised hosts, strongyloidosis result in hyper infection é colitis, enteritis or malabsorption. In disseminated disease larvae invade not only the GIT & lung, but also the CNS, peritoneum, liver &kidneys. Bacteraemia may develop from enteric bacteria entering through the disrupted intestinal mucosa.

Diagnosis

In uncomplicated strongyloidosis, the finding of Rhabditiform larvae in faeces is diagnostic & serial stool examinations may be needed. Eggs are almost never seen in stool because they hatch in intestines.

Treatment

Even asymptomatic pts should treated.

•Thiabendazole, is still the drug of choice, 25 mg/kg BID (maximum 3 gm/day) for

3 days. There are however common side effects like nausea, vomiting, diarrhoea, dizziness & neuropsychiatric disturbances.

•Ivermectin 200 µg/kg as a single daily dose for 1-2 days is better tolerated. The disseminated cases treated for 5-7 days.

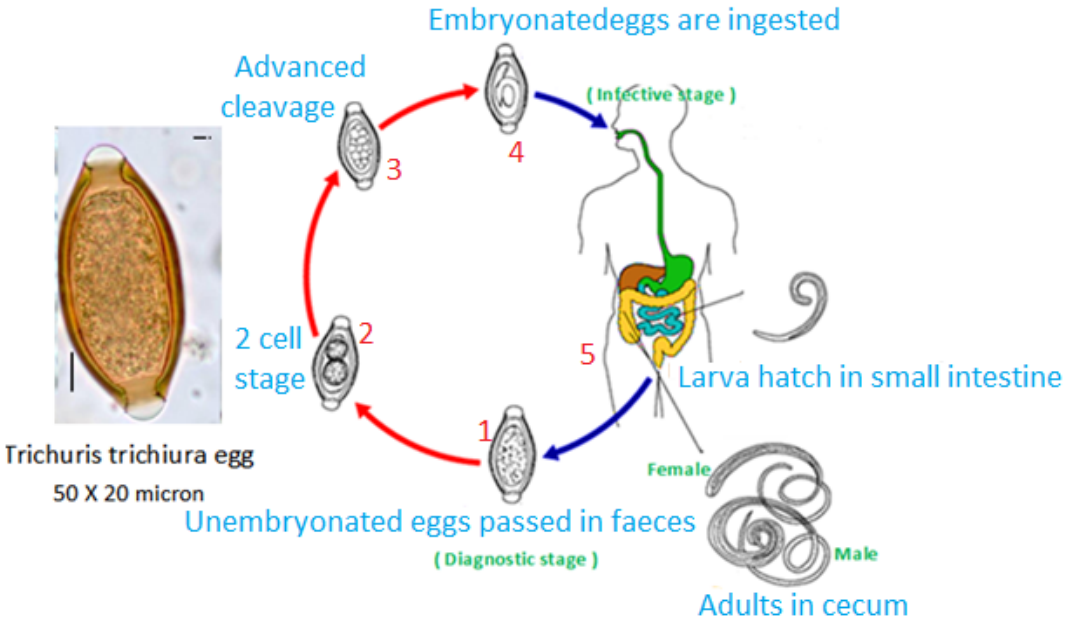
•Albendazole 200 mg/day PO for 3 days gives 100% cure rate.

TRICHURIASIS

Definition

Trichuriasis (whip-worm infection) is an infection of the human intestinal tract caused by the nematode Trichuris Trichiura. It is distributed worldwide, but is most abundant in the warm, moist regions of the world, the tropics & subtropics.

Life cycle



The parasites have a characteristic whip like shape. The anterior portion is long & thread like, the posterior portion is broader & comprises about 2/5 of the worm. Females are slightly longer than males (3-5 cm long). The adult worms reside in the colon & caecum. The anterior portions threaded into the superficial mucosa. Thousands of eggs are laid daily & pass é faeces. They mature in the soil. After

ingestion, the eggs hatch in the duodenum, releasing larvae that mature before migrating to large bowel. Adult worms may live for several years.

Clinical picture

Most infections are asymptomatic. Large worm burden may be associated especially in children é diarrhea of long duration, dysentery, mucoid stools, abdominal pain &tenderness, dehydration, anemia, wt loss &weakness. Rectal prolapse may occur, particularly in children.

Diagnosis

Demonstration of characteristic lemon-shaped eggs, or adult worms, ẃ are about 3-5 cm long, can be seen on proctoscopy.

Treatment: Mebendazole 100 mg 1 X 2 X 3 days or Albendazol 4 mg/kg.

ENTEROBIASIS

Infection of the human intestinal tract by the pinworm Enterobius Verfmicularis.

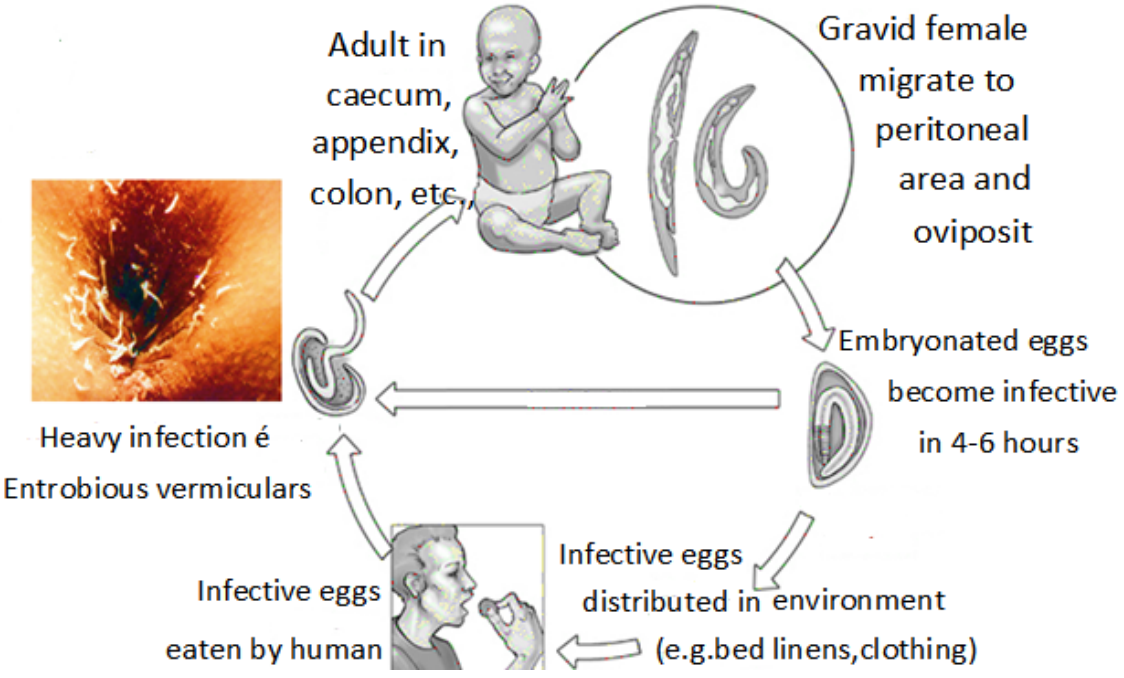
Epidemiology

Pinworms are one of the most common intestinal nematodes, cosmopolitan, more in temperate zones é about 30-50% of the population infected, more common in white than colored people, more prevalent in children than adults. Enterobiasis is most common where people live under crowded conditions as orphanages, kindergartens, primary school students & large families.

Life cycle

Adult worms inhabit the cecum & colon. Right after mating, the male dies.Therefore, the male worms are rarely seen. The gravid female worm migrates nocturnally out into the perianal region & releases up to 10.000 immature eggs. The eggs are rapidly infective & are transmitted by hand-to-mouth passage. The larvae ha-

tch, mature entirely within the intestine. Self-infection results from perianal scratching & transport of eggs to the hands or nails & then to mouth (autoinfection). Pinworm infections are very common among family members. The female worm measures 8-13 mm in size & is fusiform in shape. The male adult is 2-5 mm & the tail is curved. The egg is 50-60 X 25 µm, persimmon seed-like, colorless & transparent, thick & asymmetric shell, content is a larva. The embryonated egg is the infective stage & the life span of the worm is 1-2 months.



Clinical picture

About one-third of pinworm-infected persons are asymptomatic. The adult worms may cause slight irritation of the intestinal mucosa. Major symptom is anal pruritus, ẃ associates é the nocturnal migration of the gravid fem ales from the anus & deposition of eggs in the perianal folds of the skin. Restlessness, nervousness & irritability, probably resulting from poor sleep associated é anal pruritus. In young girls, migration of the worms may produce vaginitis, salpingitis or granuloma of the peritoneal cavity.

Diagnosis

•Microscopic identification of eggs collected in the perianal area by cellophane (Graham Scotch) tape or anal swabs. The tape is then transferred to slide to be seen under microscope. This must be done in the morning, before defecation.

•Detection of adult warm on anal skin.

•Diagnosis often made clinically by observing female worm in the perianal region.

Treatment

Since the life span of the pinworm is < 2 mon, the major problem is reinfection.

Albendazole & Mebendazol are 95% effective but do not kill eggs, 2 or more courses of treatment needed for radical cure. Also treatment of all the members of the family even adults is recommended.

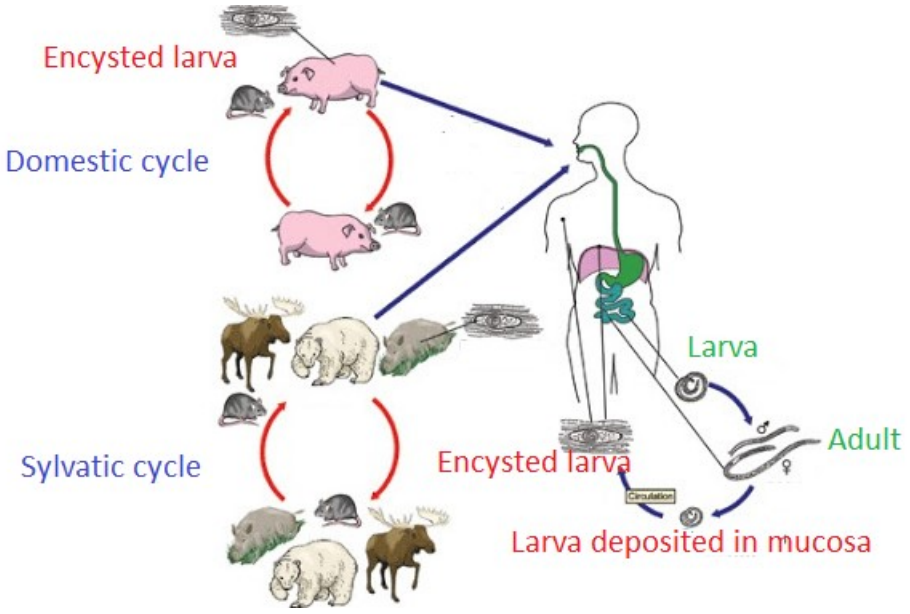
Bendax/Vermizole/Alzental 100 mg suspension, 200 mg tab., single dose 2 tsp for children < 2 years & 4 tsp for children >2 years & 2 tab for adults & to be repeated for all after 2 weeks.

Prevention: treatment of pts & carriers, health education, hygienic habits, sanitation of clothing, beading & environment.

TISSUE NEMATODES

The tissue nematodes include Trichinosis, Visceral or Ocular or Cutaneous larva migrans, Cerebral angiostrogliasis & Gnathostomiasis.

TRICHINOSIS



Disease caused by the parasite Trichinella Spiralis, characterized by acute & rapid course é fever, GIT symptoms, myalgia & eosinophilia.

Epidemiology: widely spread throughout the temperate regions of the world wherever pork or pork products are eaten. It is enzootic in wildlife in Africa & man is involved sporadically by eating fresh or inadequately cooked pork.

Life cycle

The trichina worm is white round worm just visible to the naked eye. Adult male 1.4-1.6 mm in length by 40-60 µm in diameter; the female is longer, 3-4 mm in length & about 1½ times as broad as the male. The worm gains entrance to the digestive tract as larva encysted in muscle tissue. By the time they reach small intestine, freed from their cysts, penetrate the duodenal epithelium, mature within a few days. The femaleis fertilized &produce between 1000-1500 larva during

the 3-16 wks period they parasitizes man. The larva circulates in blood, then invade different tissues mainly the muscles.

Clinical features

24 hrs following ingestion of encysted larva in undercooked meat, signs of GIT disturbances like nausea, vomiting, diarrhoea & abdominal pain may occur. With the muscular infiltration there may be periorbital oedema, myalgia & persistent fever up to 40 ^{o}C, the last stage is characterized by neurologic symptoms & sometimes myocarditis.

Diagnosis

Blood eosinophilia develops in >90% of cases, 2-4 wks after infection serum levels of IgE & muscle enzymes including CPK, LDL, & AST are ⇧ in most symptomatic pts, a presumptive diagnosis can be made based on fever, eosinophilia, periorbital oedema & myalgia after a suspected meal. Diagnosis is confirmed by ⇧ titres of parasite specific antibody or muscle biopsy demonstrating the larva.

Treatment

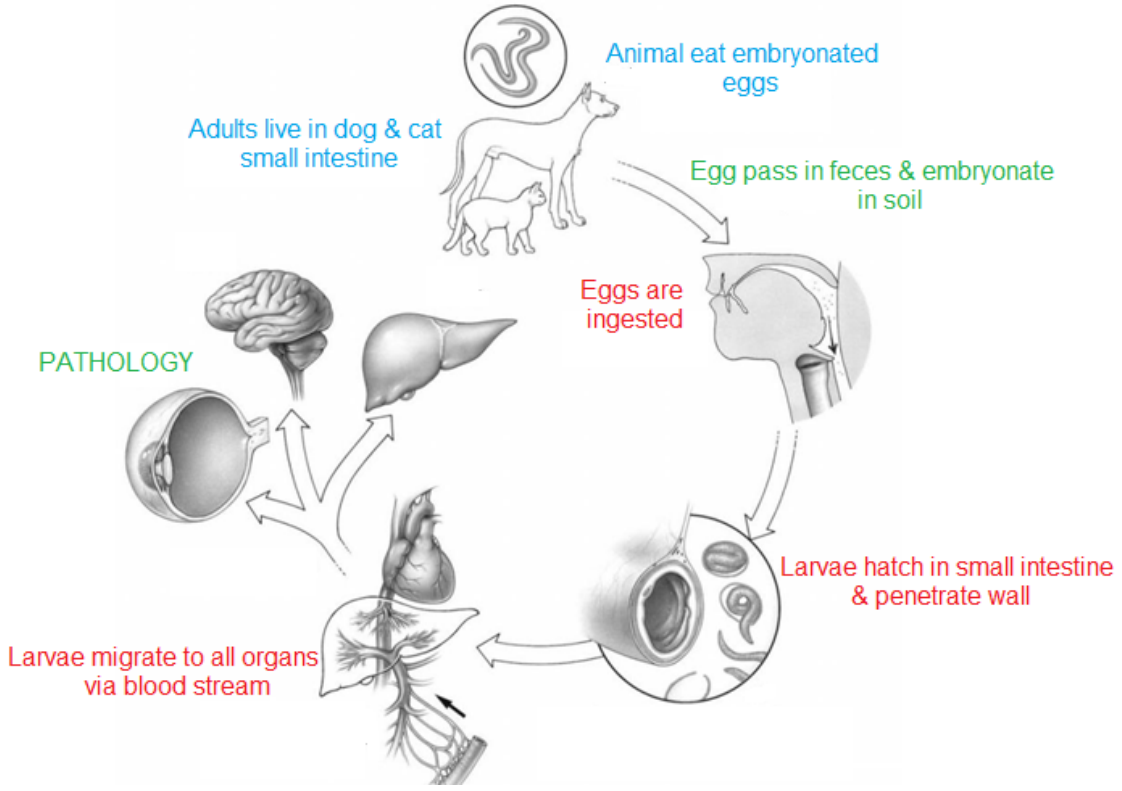
As is desirable é most diseases, early Rx is better & ⇩ the risk of developing disease. If larvae do encyst in skeletal muscle cells, they can remain infectious for months to yrs. Early administration of antihelminthics, as Mebendazole or Albendazole, ⇩ the likelihood of larval encystation, particularly if given within 3 days of infection. However most cases diagnosed after this time. Mebendazole 200-400 mg X 3 X 3 days or Albendazole 400 mg X2 for 8-14 days. These drugs prevent newly hatched larvae from developing, but should not be given to pregnant women or children < 2 yrs of age. Glucocorticoids (e.g. Prednisolone 1 mg/kg/day) are helpful for severe myositis & myocarditis.

TOXOCARIASIS

Zoonotic infection caused by the parasitic round worms commonly found in the intestine of dogs & cats (Toxocara).

Life cycle

Toxocariasis include 2 types according to the normal habitant; Toxocara canis (in dogs), Toxocara catis (in cats). The mature worm is about 6-10 cm in length. Man infected through ingestion of contaminated food or soil é feces of dogs or cats ẃ contain eggs, the egg hatches in human intestine forming larva ẃ penetrate mucosa of intestine & pass to blood to settle in different body organs.



Clinical picture

Most people infected é *Toxocara* do not have any symptoms. There are 2 major forms; Visceral Toxocariasis (VT), also called Visceral Larva Migrans (VLM), Ocular Toxocariasis (OT), also called Ocular Larva Migrans (OLM). The syndromes VLM & OLM can be caused by infection é the migrating larvae of other kinds of parasites

ẃ cause symptoms similar to those caused by migrating T*oxocara larvae.* In few people who are infected é high numbers of *toxocara larvae* or have repeated infections, the larva can travel through parts of the body as the liver, lungs or CNS causing symptoms as fever, cough, pneumonia, enlarged liver. The larva can also travel to the eye & cause OT, ẃ occurs when microscopic toxocara larva enters the eye, causing inflammation & scarring on retina resulting in visual deterioration, chorioretinitis, red eye, typically occur in one eye.

Investigations

- Detection antibodies to toxocariasis: ELISA test, sensitive up to 90%.
- CBC: shows marked ⇧ of eosinophilic count, leukocytesis.
- Immunoglobulins: hypergammaglobinaemia (IgG, IgM, IgE).
- Sonar/C-T/MRI: visualize granuloma anywhere.

Management

- Albendazole suspension 100 mg, 2-4 tsp daily for 3-5 days for children. 2 tab (200 mg/tab), daily for 3-5 days for adults.
- Steroids used to reduce inflammation & granulomatous reaction.

FILARIASIS

Filariasis is caused by Wuchereria Bancrofti, Brugia Malayi or Brugia Timori. While the later 2 are found in Asia, the former is prevalent in the tropics & subtropics. Therefore, W. Bancrofti is discussed below.

LYMPHATIC FILARIASIS

Lymphatic filariasis is due to the presence of adult W. Bancrofti in the lymphatic system or connective tissues of man. Many species of anopheles; culex, mansonia & aedes are acting as a vectors.

Epidemiology: it is widespread throughout most of the tropics & subtropics. Also found in some fareast countries. The mosquito, inoculate microfilaria into human skin, it pass to lymphatics or SC tissue where it proliferate to adult warms & in turn gives microfilaria. The adult warm length 4-10 micron & microfilaria 150-300 micron.

Clinical picture

Most of infected individuals have few symptoms despite large numbers of circulating microfilaria in the peripheral blood. But subclinical disease is common é microscopic haematuria &/or proteinuria & in men scrotal lymphangiectasia. Only few pts progre- ss to the acute & chronic stages of infection. Pt may present

acutely é high-grade fever, lymphangitis & transient local oedema. Later on pt may have lymphedema (upper & lower extremities) & scrotal swelling. Lymphatic filariasis may affect breast, vulva & may associated é 2ry bacterial infection due to impairment of blood circulation.

Diagnosis

- Demonstration of microfilaria from blood, or hydrocele fluid or other body fluids at night (because periodicity of microfilaria).
- CBC: marked eosinophilia.
- ⇧ of IgE
- ELISA for detection of antibodies against Filariasis.
- Blood film for Wucheraria bancrofti using Giemsa stain.
- Isolation of warm from fluid collection (in scrotum, legs, or breast).
- U/S of scrotum, breast for detection of the warms.

Treatment

Diethyl Carbamazepine 6 mg/kg daily for 12 days is the Rx of choice. Albendazol 400 mg twice daily for 21 days has been shown to have microfilaricidal activity.

ONCHOCERCIASIS

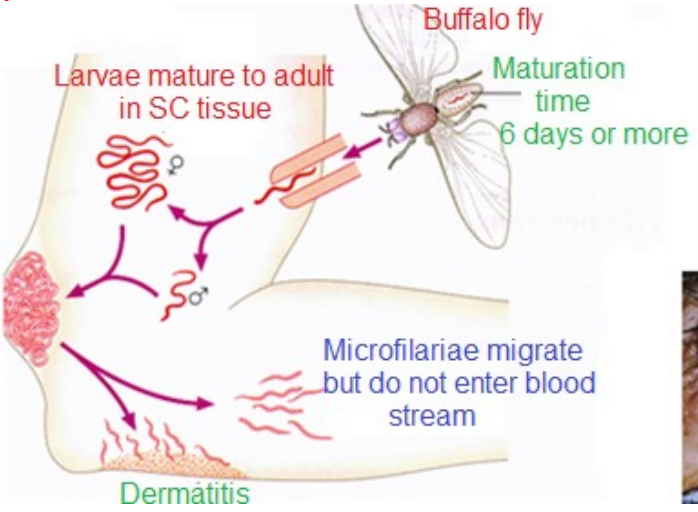
Onchocerciasis is caused by the filarial nematode Onchocerca volvulus & is spr-ead by the bite of an infected Black Fly, is also called river blindness because infections are most intense in remote African rural agricultural villages, located near rapidly flowing streams.

Aetiology/Epidemiology

Global onchocerciasis prevalence is 17.7 million. 99% of infected persons are in Africa. Is the world's 2nd leading infectious cause of blindness. The living parasites

are white or cream coloured & transparent. The males are 19-42 mm long & the females 33-50 cm long.

Life cycle



Visible onchocercal nodule

Microfilaria came out through the eye

Vector is the Black Fly ẃ breed on the sides of running river for many kilometers around the river, the fly inoculate larva into skin of man, the severity of the disease depends on the intensity of bites. The larvae maturate to adult warm male & female in the SC tissue forming a nodule. About 7 months -3 years after infection, the gravid female releases microfilariae that migrate out of the nodule & throughout the tissues, infection is transmitted to other person when female Black Fly ingests microfilaria from the host's skin, these microfilaria then develop into infective larvae. It takes about 1-3 weeks for microfilaria to develop into infective larva inside the fly & to be inoculated into another persons, the warm does not penetrate the blood stream, but migrate through SC tissue & lymphatics to different body parts.

Clinical features

Following the bite of an infected fly, there is an IP of several months before nodules appear. The SC nodules "onchocercomata" are the most characteristic lesions. Usually appear on legs, coccyx, sacrum, thigh or in bony prominences.

This granuloma may be seen anywhere in the body, may be single or multiple up to over 100 nodules, may form huge mass in the skin, associated é loss of elasticity, wrinkling of skin & epidermal atrophy that can be more often lead to hypopigmentation than hyperpigmentation & eczematous dermatitis é sever itching. Visual impairment is the most serious complication. Early lesions in the eye are conjunctivitis é photophobia, iridocyclitis, sclerosing keratitis leading to blindness. The microfilariae can be seen by naked eye coming out through the eye. Pt could have enlarged inguinal LN (hanging groin). Heavily infected pt could have severe wasting.

Diagnosis

- Demonstration of microfilariae in the skin snip or nodules. Microfilaria are rarely found in blood smear, but may be seen in urine.
- CBC: marked eosinophilia.
- PCR.
- Marked ⇧ in IgE. .

Treatment

Once a victim infected, there is no cure from the disease, but its progress can be delayed é oral medication.

Ivermectin: is the Rx of choice, PO as a single dose of 60 mg tab, ½ -2 tab, or 150 mcg/Kg (max. 120 mg), repeat every 6 months or every yr. It inhibits the production of microfilariae by adult female worms for some months, killing off almost 95% of the tiny worms. Be sure there is no Loa Loa infection as the drug may cause severe reaction. The drug has many advantages as; no severe ocular reaction & prevents blindness due to optic nerve disease by 50%, but it is contrai-

ndicated if there is coinfection é Loa Loa or pregnant or lactating women or children < 5 years.

Antihistamines: should be given for the pruritus.

Surgical excision of the nodules.

Prevention

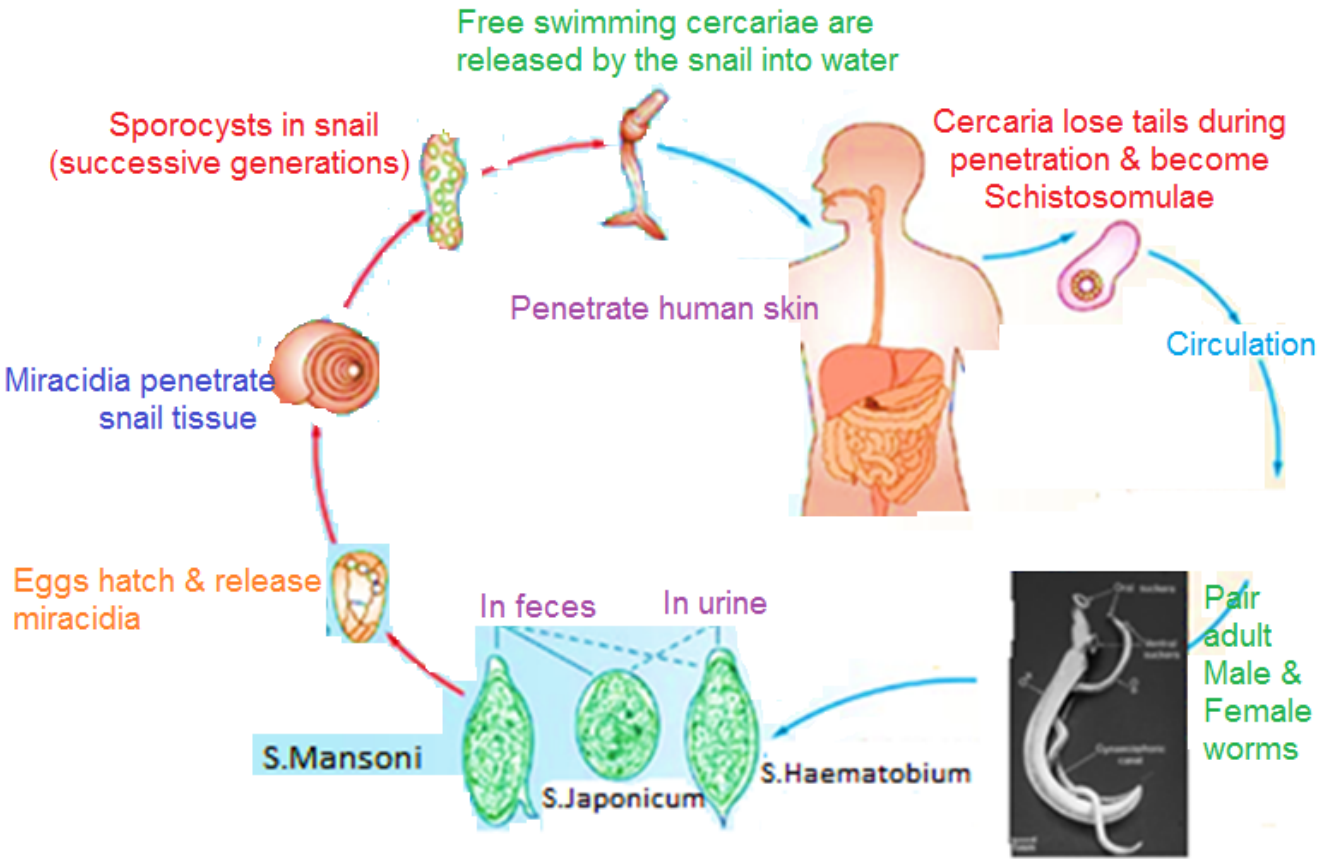
The disease is highly preventable, control based on strategies:-

- Vector control by spraying insecticides, controlling insect breeding sites in rivers is one of the pillars of prevention by spraying the aerial spaces & rivers.
- Personal exposure in endemic areas can reduced by avoiding black fly localities & by protective clothing.
- Repellents are of value only for short periods as they are washed off by sweat.
- Free distribution of the highly effective medicine-Mectizan (Iverectin), this medication provides a yearly protection from a single dose (Levine, 2007). Diethylcarbamazine is contraindicated because it is associated é severe & fatal post treatment reaction.

TREMATODES

Trematodes or flatworms are a group of morphologically & biologically heterogenous parasitic helminths that belong to the phylum platy helminthes. Human trematode infections are classified according to the site they involve; the adult flukes may involve blood, biliary tree, intestines or lungs. Blood flukes are Schistosoma Mansoni, Hematobium, Japonicum, Intercalatum & Mekongi. Biliary flukes are Opisthorchis Viverini, Clonorchs Sinensis & Fasciola Hepatica. Intestinal flukes are Fasciolopsis Buski, Heterophyes. Finally, lung flukes are Paragonimus Westermani. Because of its public health importance, only Schistosomiasis is discussed here.

SCHISTOSOMIASIS



Schistosomiasis (Biliharziasis) is a group of diseases caused by the genus schistosoma affecting mainly the GIT & genitourinary organs.

Geographical distribution

- Sch. Haematobium: in Middle East & Africa.
- Sch. Mansoni: is found in Middle East, Africa, South America.
- Sch. Japonicum: in Japan & Far East.
- Sch. Mekongi & Sch. Intercalatum: are found focally in South East Asia & Central West Africa.

Sch.Haematobium is the cause of urinary Schistosomaiasis while all the rest cause intestinal Schistosomiasis.

Life cycle

Man is the definitive host where sexual reproduction takes place after cercarial entry by skin penetration. Snails are the intermediate hosts in ẃ asexual regeneration continues. Each species of Schistosoma has a specific snail host. The parasite eggs released into fresh water (from human urine or feces according to species). Eggs hatch giving rise to the ciliated miracidia (free swimming). Miracidia find & infect snail host (different species prefer different snail species), each miracidia transforms into many fork-tailed, free swimming forms (Cercariae) within 4-6 wks of entering snail. The cercariae leave snail &move into water for up to 18 days. When cercariae find a human host, it the penetrate skin & differentiate into larval forms called-Schistosomulae. Schistosomulae migrate through the host's skin, gain access to the lymphatic system, travel to the lungs (stay 3-8 days), then migrate to liver portal system where they mature into adult worms. Male & Female adult worms in liver pair up, female inserts herself into the gynecophoral canal of male, they are now 'paired', migrate to favoured sites according to species:-

- Sch.Haematobium migrate to perivesical venous plexus surrounding the bladder
- Sch. Mansoni migrate to mesenteric venules of large bowel & rectum.
- Sch. Japonicum migrate to mesenteric veins of the small intestine.

S. mansoni - Biomphalaria species.

S. haematobium - Bulinus species.

S. japonicum - Onchomelania species.

Clinical picture

Intestinal schistosomiasis is caused by all human Schistosoma except Sch. Haematobium, ẃ is the only cause for urinary Schistosomiasis. It affects the large bowel, the liver (intestinal form), manifestations are dependent on the stage of infection. The following first 2 stages are the same for all species & the 3rd stage is different:-

First stage: swimmer's itch (invasion): is the first clinical sign of acute infection appearing soon after exposure, usually within 24-48 hrs & characterized by itching at sites of cercarial entry. Seen in new comers & not common in indigenous people.

Second stage: acute stage (toxemia). It is an early allergic manifestation to egg deposition in response to massive antigenic stimulus of eggs. Include fever, headache, chills, myalgias, profuse diarrhea, nausea & vomiting. Pt may have generalized lymphadenopathy, heapatosplenomegaly, urticaria & leucocytosis é marked eosinophilia. Severity depends on intensity of infection & tends to be mild in indigenous population. Such clinical manifestations come out after 4-8 weeks of infection, similar to the time from egg to adult worm (40 days).

Third stage: is the chronic stage, occurs 3 months to several years later, coincides é deposition of eggs in the tissues. The clinical picture represents the effect of the pathologic lesions caused by the eggs on the urinary & GIT systems. Differ in their manifestations, as follow:-

i) Intestinal Schistosomiasis: the disease is very light & symptomless for months, then presenting é recurrent bloody diarrhea & lethargy. They may have intestinal polyps &progressive fibrosis of the intestinal wall leading to formation of strictures but intestinal obstruction is rare. Moreover, granulomatous hepatitis followed by progressive periportal fibrosis (also called pipe stem fibrosis) may develop resulting in portal hypertension é splenomegaly, ascites & oesophageal varices.

ii) Urinary Schistosomiasis: eggs deposition in the wall of urinary bladder induces the formation of pseudo tubercles & epithelial hyperplasia é subsequent fibrosis & calcification causing dribbling, incontinence, frequency, dysuria & hematuria. Chronic infection leads to obstructive uropathy, hydronephrosis, chronic pyelonephritis, renal failure & contraction of the bladder. Rarely the gonads, CNS "brain, spinal cord", lungs & endocrine organs may involved by egg deposition.

Diagnosis

- Identification of the characteristic ova in stool or urine by direct smear method; easy but light infection can be missed.
- Rectal snip/bladder biopsy if it cannot be detected in stool or urine.
- Antibody detection; the most frequently used technique is ELISA, but antibody levels do not differentiate between past & present infection & do not give any information about intensity of infection, therefore, can`t be used as cure monitor.
- Circulating antigen assays: acts as a reliable cure monitor.

Clinical diagnosis

Intestinal schistosomiasis

- Sigmoidoscopy & rectal snip: identifies lesions & ova of the parasite.
- U/S of liver & spleen: demonstrate periportal fibrosis & spleen enlargement.
- Liver biopsy

Urinary schistosomiasis

- Cystoscopy: demonstrates fibrosis & calcification of the bladder, bladder biopsy & histology demonstrates ova.
- Plain abdominal X ray may detect bladder calcification.
- IV pyelogram to see for the presence of obstructive uropathy.
- Renal U/S .

Treatment

Drug treatment is both safe &effective. Praziquantel: has wide spectrum, effective against all species, single dose, has high cure rate. The dose for Sch. Mansoni & Haematobium is 40 mg/kg & for Sch. Japonicum is 60 mg/kg.

Prevention

Prevention & control requires multidisciplinary approach:

- ***Environmental sanitation***: avoidance of pollution of surface water; provision of latrine & sanitary waste disposal, prevention of human contact é infected water, provision of safe & adequate water, protective clothing when contact is unavoidable, health education.
- **Elimination of the disease**: in the reservoir by chemotherapy. Case finding & Rx & mass Rx in selected population.
- ***Snail control***: eliminating the water-born snails ẃ are natural reservoirs for the

disease, usually done by identifying bodies of water, as lakes, ponds, ẃ are infested. Snail control include;

-Physical control: removal of vegetation, drainage of swamps.

-Chemical control (molluscicides) to the water in order to kill snails.

-Biological control by using fish or other snails that feed on vector snails.

CESTODES

Cestodes (tapeworms) are segmented worms. Tapeworms can divided into two. In one group the definitive hosts are humans, these include: Taenia saginata, Diphylobt-hrium, Hymenolepsis & Dipylidium Canium. In the other group, humans are intermediate hosts, these include: Echinococcosis, Sparganosis & Coenurosis. Humans can be a definitive or intermediate host to T.solium.

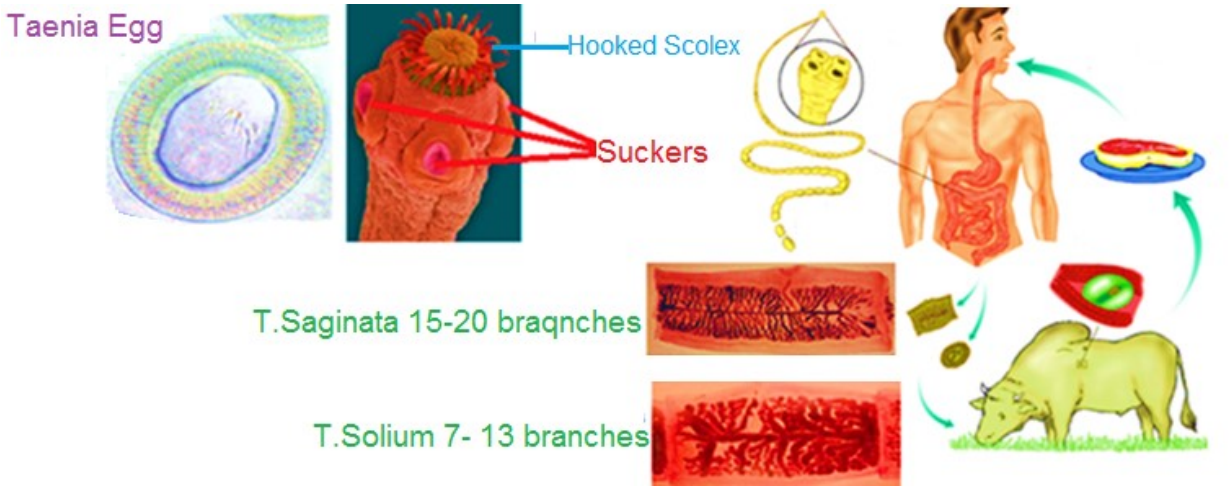
TAENIASIS SAGINATA

Taeniasis Saginata (beef tapeworm) infection is caused by the presence of the adult beef tapeworm, in the intestine of humans.

Distribution

It is found all over the world. Occurs in all countries where raw-meat is ingested. Prevalent in sub-saharan Africa & Middle East.

Life cycle



T. Saginata is a large tapeworm usually 5-10 meters in length. The scolex carries 4 round suckers. Behind the scolex there is a short neck from ẃ proglottids (segm-ents) form. Each proglottid matures, it is displaced further back from the neck by the formation of new, less mature segments. Humans are the only definitive

host. Eggs deposited on vegetation can persist for months or yrs, until ingested by cattle. Embryo from cattle intestine migrates to the muscle &transform into cysticercus. When eaten

raw/undercooked meat, this cysticercus infects human.

Clinical picture

Usually pt is asymptomatic & often infection is detected when pt pass proglottids é stool or alone. Abdominal pain, nausea & wt. loss can occur.

Diagnosis

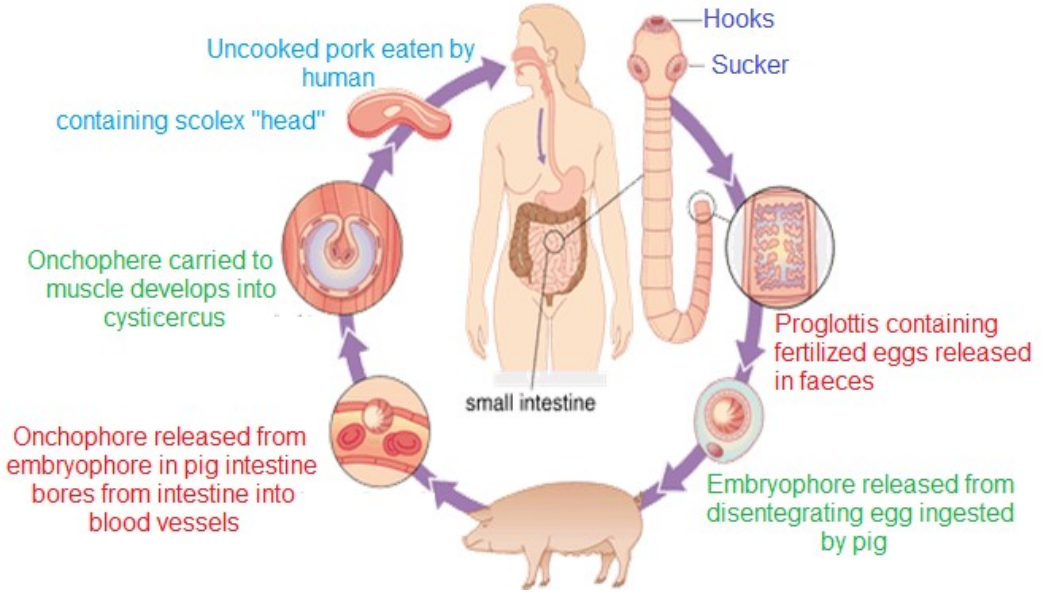
- Demonstrating the eggs or proglottids in pt`s stool.
- Each gravid proglottids of **T. Saginata** passed in stool (approximately 6 proglottid/day) may produce up to 100.000 eggs.

Treatment

Prazequantel 5-10 mg/kg in a single dose or

Niclosamide 2 gm as single morning dose before breakfast as alternative.

TAENIASIS SOLIUM



It is caused by T. Solium from eating raw or undercooked pork.

Etiology

The adult tapeworm resides in the upper jejunum, similar to T. Saginata. Its scolex attaches to intestinal wall by both sucking disk & 2 rows of hooklets.

Life cycle

T. Solium has a very similar transmission pattern to T. Saginata. Humans are the only known definitive host. Infection begins é the ingestion of infected raw or undercooked pork. The T. Solium larvae gets digested out of the meat & attaches itself to the upper small intestine. In the small intestine it will mature & ⇧ its number of proglottids. Terminal gravid proglottids will break off from the main body & will either pass out é stool or worm its way out of the anus. In certain cases, 3-4 attached proglottids will pass out together. The eggs housed in the proglottids will be released & remain viable in the soil for wks, single proglottid may produce 50,000 eggs. However, unlike T. Saginata, both pigs & humans can become intermediate hosts to the T. Solium. When pigs & humans ingest the eggs, the oncospheres will pierce through the intestinal walls, travel through the circulatory system, plant itself in SC tissue & muscles such as the brain & eyes. Cysticercosis will develop in these areas &become infective in 9-10 wks. Pigs will die in several months. In humans, cysticercosis has a variety of damaging effects on the CNS, vision & brain. In humans, autoinfection of T. Solium eggs can occur by reverse peristalsis of the intestine. Similar to beef tapeworm. However, both the adult tapeworm & the larvae (cysticerca) infect people.

Clinical features

Mostly the pts are asymptomatic; but they could have epigastric discomfort, nausea & wt. loss. Pt may note passage of proglottids in stool. When infected é

cysticerica (cysticercosis), they are distributed all over the body. The major manifestations come from the CNS é seizures, headache, ⇧ ICP & mental changes

Diagnosis

Detection of eggs or proglottides in stool.

Diagnosis is difficult in cysticercosis ẃ is done by different clinical & lab. criteria.

Treatment

Prazequantel, single dose 5-10 mg/kg.

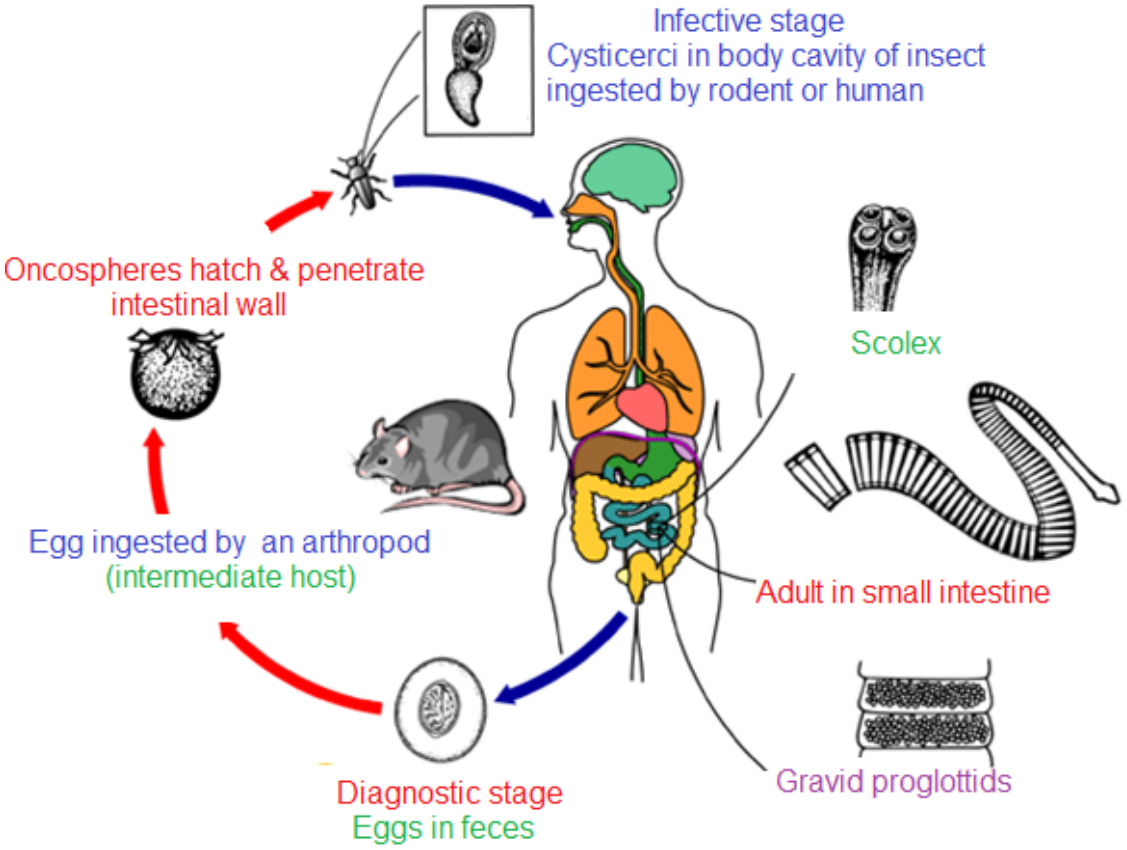
HYMENOLEPIS NANA

Commonly called the dwarf tapeworm “Nanos=dwarf”.

Epidemiology

One of the most common cestodes, infecting human, especially children.

Life cycle



Dwarf tapeworm is 25-40 mm in length X 1 mm in breadth. The scolex bears 4

small suckers. Eggs measure 30-47 microns in diameter, they are round to oval & should contain a 6-hooked oncosphere (useful in diagnosis under the microscope & differentiation of parasite eggs), also they have polar filaments that lie between the egg shell & the oncosphere. Definitive hosts are human, mice, rats. Intermediate host (optional): fleas & beetles. H. Nana is the only cestode that parasitizes humans éout requiring an intermediate host. Eggs of H. Nana are immediately infective when passed é stool & can`t survive **>** 10 days in the external environment. Human infection occur as a result of:- accidental ingestion of tapeworm eggs, or ingestion of fecally contaminated foods & water or by touching mouth é contaminated fingers or by ingestion of contaminated soil & also when eggs ingested by an arthropod intermediate host where they develop into cysticercoids, ẃ can infect human or rodent upon ingestion. When eggs are ingested (food, water, hands, arthropod intermediate host) the oncospheres contained in the eggs are released. The oncospheres penetrate the intestinal villus & develop into cysticercoid larvae. Upon rupture of the villus, the cysticercoids return to the intestinal lumen, evaginate their scoleces & attach to the intestinal mucosa where they develop into adults that reside in the ileal portion of the small intestine producing gravid proglottids. Eggs are passed in the feces when released from proglottids after the proglottids disintegrate in the small intestine. An alternate mode of infection consists of internal autoinfection, where the eggs release their oncospheres, ẃ penetrate the villus continuing the infective cycle éout passage through the external environment. The life span of adult worms is 4-6 wks, but internal autoinfection allows the infection to persist for years.

Clinical features: most infections are asymptomatic. Severe infections may manifest é abdominal pain, anorexia & diarrhea.

Diagnosis: based upon demonstration of the eggs in the stool.

Treatment: Praziquantel 25 mg/kg as single dose is the Rx of choice. A course of Niclosamide for 7 days is also effective.

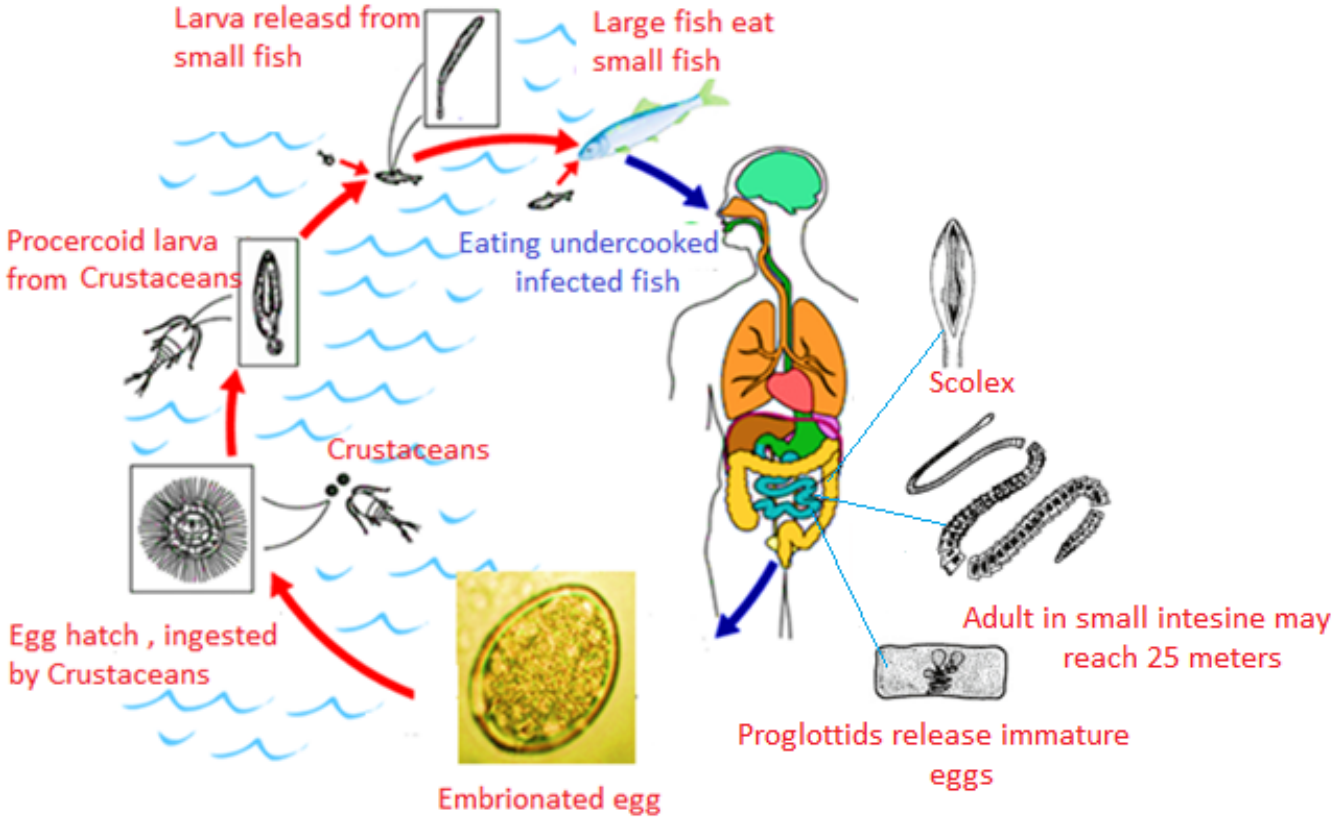
Prevention: Good hygiene, elimination of rats & mice, a well-balanced diet to promote resista- nce to infection, public health & sanitation programs.

DIPHYLLOBOTHRIASIS

Etiology/Epidemiology

Diphyllobothriasis is infection caused by adult diphyllobothrium latum. It is acquired from eating raw fish. Diphyllobothriasis occurs in the Northern Hemisphere (Europe, North America & Asia) & in South America (Uruguay & Chile).

Life cycle



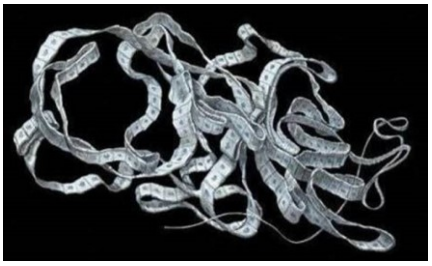
Immature eggs are passed in feces. Under appropriate conditions, the eggs mature (approximately 18-20 days) & yield oncospheres ẃ develop into a coracidia. Aft er ingestion by suitable freshwater crustacean (copepod first intermediate host) the coracidia develop into procercoid larvae. Following ingestion of the copepod by a suitable second intermediate host, typically minnows & other small freshwater fish, the procercoid larvae are released from the crustacean & migrate into the fish flesh where they develop into a plerocercoid larvae (sparganum). The plerocercoid larvae are the infective stage for humans. Because humans do not generally eat undercooked minnows & similar small freshwater fish, these do not represent an important source of infection. Nevertheless,these small second intermediate hosts can be eaten by larger predator species, e.g. trout, perch, walleyed pike. In this case, the sparganum can migrate to the musculature of the larger predator fish & humans can acquire the disease by eating these later intermediate infected host fish raw or undercooked. After ingestion of the infected fish, the plerocercoid develop into immature adults & then into mature adult tapeworms ẃ will reside in the small intestine. The adults of D. latum attach to the intestinal mucosa by means of the 2 bilateral groves (bothria) of their scolex. The adults can reach >10 m in length, ē > 3,000 proglottids. Immature eggs are discharged from the proglottids (up to 1,000,000 eggs per day per worm) & are passed in the feces. Eggs appear in the feces 5-6 wks after infection. In addition to humans, many other mammals can also serve as definitive hosts for D. latum.

Clinical Picture: many people are asymptomatic. But pt. could have abdominal pain, loss of appetite, anorexia, nausea, diarrhea or loss of weight. Since this tap

worm consumes a lot of Vit. B_{12} & interferes é its absorption, it can cause Vit. B_{12} deficiency (megaloblastic anaemia).

Treatment

Praziquantel 5-10 mg/kg once is very effective. Vit. B_{12} deficiency should be treated if present.

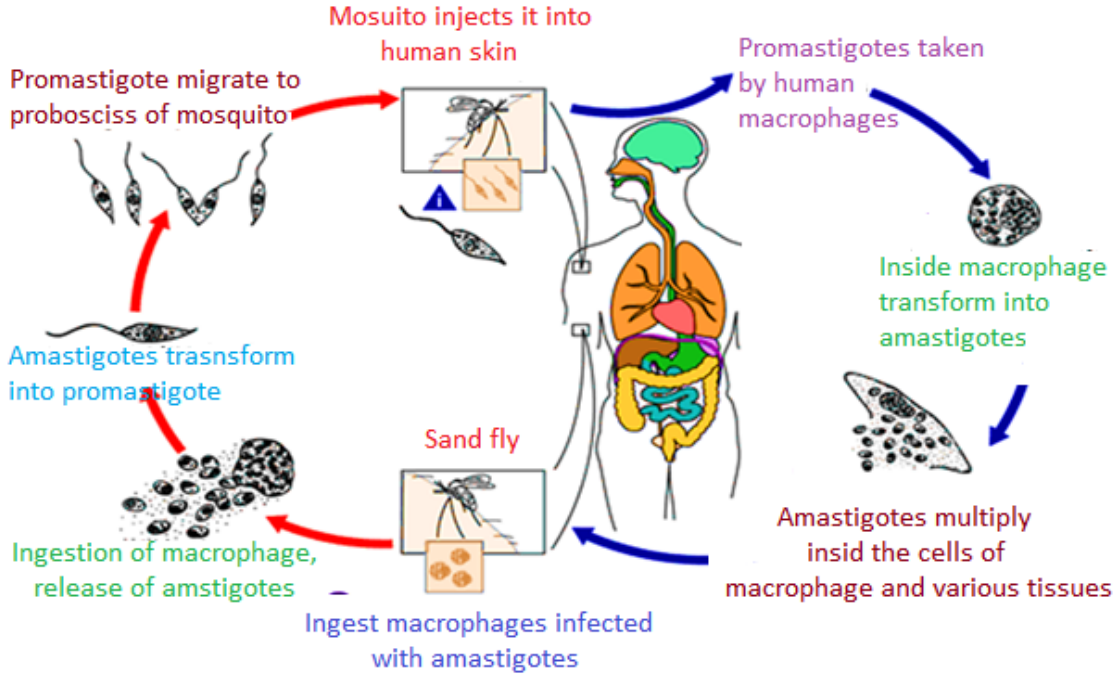


LEISHMANIASIS

Infectious disease caused by the protozoa called *Leishmania.* Leishmaniasis transmitted to man from animals through *Sand Fly.* There are 3 major clinical forms :-

Visceral, Cutaneous & Mucocutaneous leishmaniasis.

Life cycle



Life cycle starts when parasitized female sand fly takes a blood meal from a human host (sand fly is very small, may be hard to see, they are 1/3 size of typical mosquitoes, fly éout making any noise). As the sand fly feeds, **promastigote** forms of the leishmanial parasite (the flagellated forms) enter the human host via the proboscis. Within the human host, the promastgote forms are ingested by macrophage where they metamorphose into **amastigote** forms (non flagellate form), reproduce by binary fission & ⇧ in number until the cell eventually bursts, then infect other phagocytic cells & continue the cycle. The IP of leishmaniasis varies from weeks to years. If infected host is bitten by another female sand fly, the parasites are taken up by the fly during the blood meal, transformed inside the fly & delivered to new host & lifecycle continues.

VISCERAL LEISHMANIASIS

Epidemiology: Visceral leishmaniasis (Kala Azar).affects many countries in Africa, mainly Ethiopia, Sudan, Middle East, southern Soviet Union, India & south America. The disease is becoming a common opportunistic infection in AIDS.

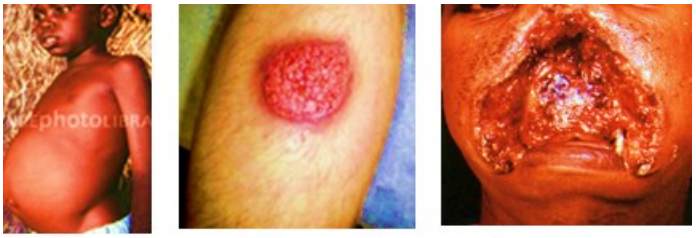
Transmission: the commonest way of transmission is by inoculation of promastigotes into hum- ans by the bite of the Sand Fly ẃ breed in termite hills & forests. The source of the aflagellate forms may be either humans or extra human vertebrate reservoirs & the disease may have life cycles that involve humans & sand flies only, or humans, sand flies & extra human vertebrate reservoirs together. Rarely transmission may occur via blood transfusion or injections.

Pathogenesis: the common site of entrance is the skin where primary cutaneous lesion appears at the sites of sand fly bite. The lesion is tiny, may pass unnoticed. This is also called primary leishmanioma. Here a cellular reaction by lymphocytes & plasma cells develop around the amastigote- filled histiocytes in the dermis. As the immune response develops epitheloid & giant cells appear, followed in some pts by healing & in some others -usually 4-6 months later- the amastigotes escape to the blood in macrophages, leading to haematogenous spread & colonization of the cells of RES , where they multiply further, released after rupture of the cells & transported to new cells. The cells affected include that of spleen, liver, bone marrow & lymphatic glands, where the parasite multiplies & cause overcrowding of cells & as a result these organs are enlarged. Spleen is grossly enlarged é smooth capsule initially, ẃ become thickened & nodular as the disease progresses. The involvement of bone marrow leads to the development of pancytopenia. The liver é its Kuppfer cells packed é amastigotes is enlarged é re-

sultant progressive cirrhosis. The LNs are enlarged & congested especially the mesenteric LNs.

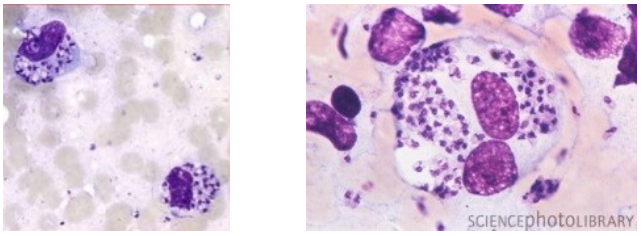
Clinical features

Visceral infections remain subclinical or become symptomatic é acute, subacute or chronic course. The onset is often gradual but can be sudden é high grade fever (intermittent or remittent) lasting for 2-6 wks. In those é gradual onset in endemic areas discomfort below left costal margin is common due to enlarged spleen & have cough, epistaxis & diarrhoea. The pt will be markedly emaciated é hepatosplenomegaly, generalized peripheral lymphadenopathy & marked pallor in the late stage of the disease. Oedema of the legs, brittle dry hair, Hge from any site (gum, skin etc.) é purpura & petechiae of the skin may occur. Some pts develop post-kala Azar dermal leishmaniasis after months or years of Rx for visceral leishmaniasis.



Visceral Cutaneous Mucocutaneous

Diagnosis



L. Donovani amastigotes (3 um) inside WBCs in blood (left) & in tissues (right).

Definitive diagnosis is based on demonstration of the parasite by:-

- Giemsa stained smear of peripheral blood.
- Culture of tissue aspirates taken from the spleen, BM, liver or LNs.

•Serologic diagnosis – ELISA or DAT, both 100% sensitive & specific.

•Montenegro skin test is -ve in visceral leishmaniasis, becomes +ve 6-8 wks after recovery •CBC- pancytopenia.

Management

Is difficult to treat. Rx include; Pentavalent antimony compounds, 20 mg/Kg/day IV or IM for 28 days or Miltefosine 50 mg capsule 1 X 2 X 28 days (approved by FDA 2014). The supportive Rx include; Blood transfusion to correct anaemia, Rx of any additional infection, & correction of malnutrition.

Prevention

•Reduction of human contact é sand flies; using insecticide impregnated bed nets. Wearing protective clothing, covering as much skin as possible.

•Chemical repellents applied on exposed skin before hours of sand fly activity (dusk & night) are effective.

•Combustion of Permethrin containing mosquito coils & Screening doors.

•Reduction of sand fly population, through using insecticides.

•Control of reservoir- dogs, rodents.

•Construct huts/camps away from breeding sites (hills & forests) & destroying of sand fly breeding sites.

CUTANEOUS LEISHMANIASIS

Oriental sore, the skin is one of the organs commonly affected by leishmania. Following the bite of sand flies, leishmania multiply in the macrophages of skin. Single or multiple painless nodules occur on exposed areas of the body, within 1 week-3 months of the bite. The nodules may enlarge & ulcerate é erythematous raised border & overlying rust ẃ may spontaneously heal over months to years.

Investigation

•Giemsa staining of smear from a split skin: Leishmania in 80% of cases.

•Culture followed by smear.

•Leishmanin skin test +ve in >90% & -ve in case of diffuse cutaneous leishmaniasis.

Clinical patterns according to etiology

In the old world			
Species	**Distribution**	**Reservoir**	**Clinical Pattern**
L.Major L.Tropica	Russia, Eastern Europe, Middle east, Meditrra-nean,subSahara & west Africa	Desert rodent for L. major. Dog &humans for L. tropica.	Spontaneous healing é scaring
L. Ethiopia	Highlands Ethiopia	Hyrax	Spontaneous healing within 6 month
In the new world			
L. Amazon			Diffuse cutaneous leishmaniasis ,resembling lepromatous leprosy(spares nasal septum)
L. Peruvia	Cooler climates		Single/multiple ulcers, heal spontaneously
L. Mexican	Mexico, Guatemala Brazil, Venezuela & Panama.		Infection of Pinna (chiclero`s ear),causes de-struction of Pinna, lesion persisting>20 yrs.

Treatment

Small lesions don't require Rx. However large lesions or those on cosmetically im-portant sites require Rx either:- •Locally-by surgery, curettage, cryotherapy or hyperthermia. or •Systemic Rx: drugs like Pentostam. Rx is less successful than visceral leishmaniasis as the antimonials are poorly concentrated in skin.

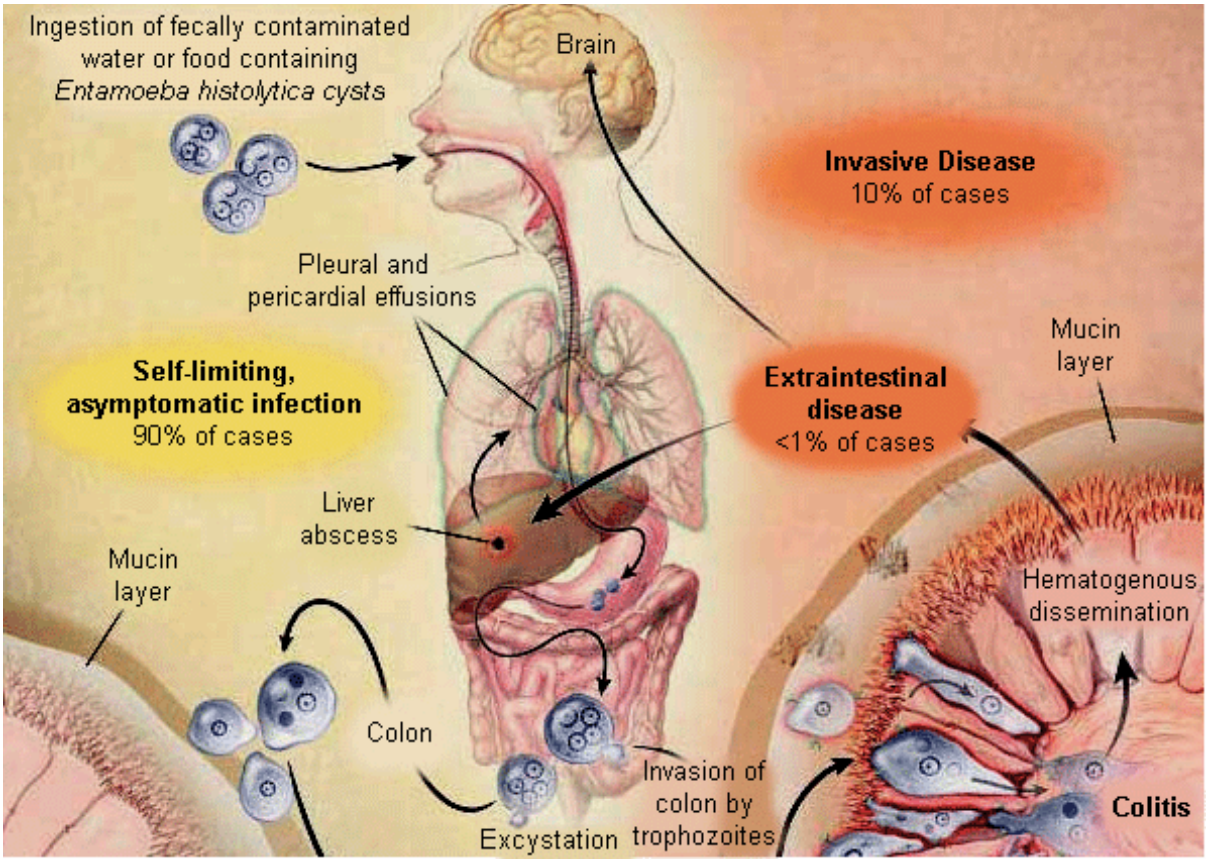
MUCOCUTANEOUS LEISHMANIASIS

Caused by L. Braziliensis, commonly seen in Latin America. In the early stage it affects the skin, but in the secondary stage of the disease it involves the upper respiratory mucosa. Present initially é painful, itchy nodules appear on the lower lim-bs then ulcerate é lymphangitis. The lesion may heal spontaneously in 6 months. In about 40% of pts the secondary lesions appear several yrs later at the mucocutaneous junctions of nasopharynx. This leads to nasal obstruction, ulcer-ation, septal perforations & destruction of the nasal cartilage called “Espundia”.

Diagnosis: •Leishmanin skin test is often +ve. •Antibody tests (ELISA) often +ve.

Treatment: Requires systemic antimonials (Pentostam) but relapses common.

AMOEBIASIS



Is a major health problem. Infection é protozoa Entamoeba histolytica. 90% of

infection are asymptomatic *A person may carry the pathogen éout evidence of the disease (asymptomatic cyst passers)* & 10% have clinical symptoms ranging from dysentery to abscess of liver/other organs. Amoebiasis is the second leading cause of death among parasitic diseases. The parasite exist in 2 forms; cyst (infective form) & trophozoite stage (invasive disease).

Life cycle

Infection occurs following ingestion of amoebic cyst (infective form); this is usually via contaminated food or water. Cysts can remain viable in the environment for wks to months & ingestion of a single cyst is sufficient to cause disease. The cysts pass through the stomach to the small intestine where they excyst to form trophozoites (form that causes invasive disease). Trophozoites graw & reproduce in intestinal tract, invade & penetrate mucosa barrier of the colon causing tissue destruction & ⇧ intestinal secretions & can lead to bloody diarrhea.

Clinical presentation

- Asymptomatic intestinal infection (carriers, passing cysts).
- Mild to moderate disease (non-dysenteric colitis).
- Severe intestinal infection (dysentery).
- Hepatic abscess.
- Ameboma (localized granulomatous lesion of colon).

Diagnosis

- ***Stool analysis:*** demonstration of cysts or trophozoites suggest amebiasis of colon. - ***Antibody detection:*** ELISA test detects antibody specific for E. Histolytica in approximately 95% of pts é extra-intestinal amebiasis & 70% of pts é active intestinal infection & 10% of asymptomatic person who are passing cysts of E.Hi-

stolytica. •***Indirect Hemagglutination test:*** +ve in 90% of pts.

Management

Amoebiasis: sometimes is a difficult disease to treat because of its tendency to chronicity & the inability of various drugs to eradicate the cystic forms of the parasite completely.

Amoebic dysentery: Metronidazole (Flagyl) tab 500 mg tds & syrup for children, 125 mg/tsp, 15 mg/Kg/Day for 5-7 days, is the drug of choice, very effective in killing amoebas in the wall of intestine & blood & liver abscesses. Almost 90% of pts é moderate amoebic dysentery responds clinically to oral Metronidazole.

need IV injections of Metronidazole (500 mg /100 ml bottle).

Asymptomatic cyst passers & chronic amoebiasis: Diloxanide furoate tab (Amoebyl) 500 mg 3 times daily for 10 days kills trophozoites & cysts in the lumen of the intestine. A combination of Diiodohydroxyquinoline 1.8 gm daily &Tetracycline 1 gm daily in divided doses for 10 days. or Furazole + Colimex suspension 1 tsp each X 3/day for 10 days. Chronic amoebic colitis is sometimes difficult to treat & usually more than one drug given in rotation.

Hepatic Amoebiasis: Metronidazole is the drug of choice. Emetine Hydrochloride & Chloroquine Diphosphate also effective. Surgery may be necessary in amoebic liver abscess & should be followed by luminal amoebicide course.

GIARDIASIS

Giardia Lamblia is a flagellated protozoan that infects the duodenum, small intestine, bile ducts & gall bladder, causing Giardiasis.

Cosmopolitan in distribution é prevalence ranges from 2-70% in populations.

The infective stage is the cyst.

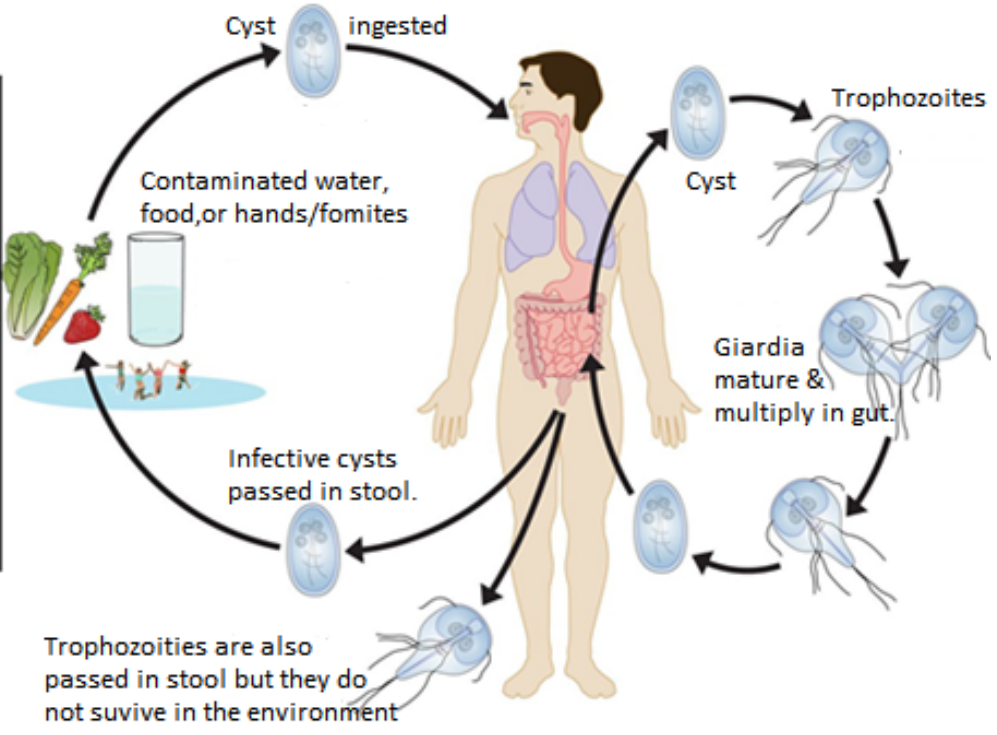
The mode of infection is through contaminated food or water, flies, food handlers (faecooral route) & hands/vomite.

Life cycle

Trophozoite stage: trophozoites attach to epithelial cells, not penetrating mucosa, feeds on mucous that forms in response to irritation, also absorbs vitamin & amino acids, interferes é lipids, vitamins & nutrient absorption:- Vit. A deficiency affect vision. Vitamin D deficiency may lead to rickets.

Cyst stage: cysts may remain viable in external environment (usually water) for many months, as few as 10 cysts can cause disease & up to 900 million cysts can be released by an infected person in one day.

Giardia-Trophozoite-Electronic Microscope.



Clinical features: IP is 1-2 wks, is of gradual onset, & may present é nausea, vomiting, watery diarrhea, dehydration, malaise, flatulence, low-grade fever & steatorrhoea. Its sequely include; malabsorption, lactase deficiency, wt loss, fatigue & rarely arthritis.

Diagnosis

•Fecal examination: water like feces (associated é trophozoites), formed feces (associated é cysts), at least 3 exams -one every other day - before judge negative

•Duodenal fluid or bile examination.

•ELISA tests: detect soluble antigen (trophozoites).

•PCR analysis: detect giardia DNA from both trophozoites & cysts.

Treatment

Metronidazole tab 500 mg tds (infusion 500mg/100ml solution) & for children syrup 125 mg/tsp, 15mg/ Kg/day for 5-7 days is the drug of choice, or

Furazoldine 2 mg/Kg X 6 hrs X 7-10 days, or

Quinacrine HcL 2 mg/Kg X 8 hrs X 5-10 days.

MALARIA

Aetiology: Protozoal disease transmitted to man by the bite of the female anopheles mosquitoes. Malaria is caused by the protozoan genus plasmodium. 4 species are known to cause disease in man:-

P. Falciparum: also called malignant malaria.

P. Vivax: tertian malaria.

P. Ovale: tertian malaria.

P. Malariae: quartan malaria

Almost all deaths are caused by P. falciparum.

Epidemiology: Malaria is one of the commonest infectious diseases of man, one of the oldest known diseases, King Tut died of Malaria? 40% of the world's population lives in endemic areas. 300-500 million clinical cases per yr. 1.5-2.7 million deaths per year (of them 90% in Africa). The prevalence of malaria is increasing

because of the emergence of DDT resistant anopheles mosquitoes, drug resistant plasmodia & the global weather changes. Transmission is common in lowlands during rainy season, especially é migration of non-immune individuals to these areas. Rare cases of congenital transmission are known. Endemicity of malaria is defined based on ***splenic rates*** (palpable spleen) in children between 2-9 years. Depending on this, regions are classified into 4 endemicity areas:-

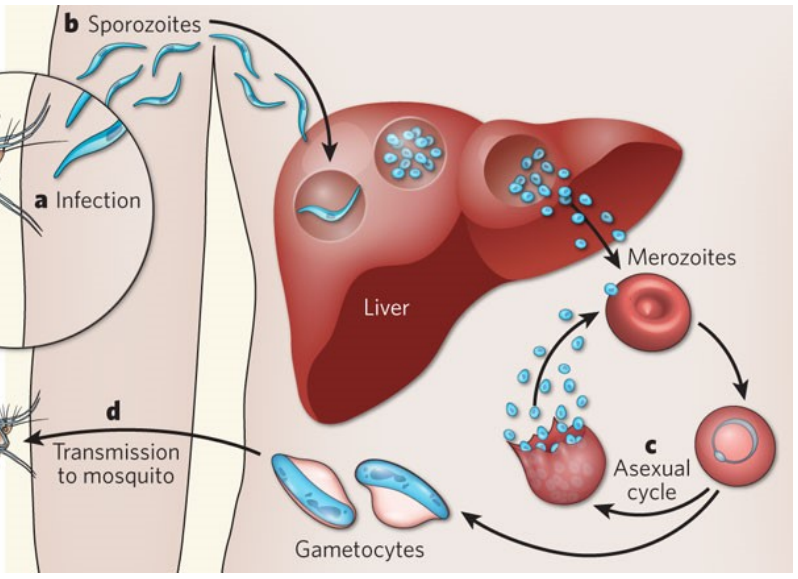
- Hypo endemic- where < 10% of children has enlarged spleen.
- Meso endemic- where 10-50% of children have enlarged spleen.
- Hyper endemic-where 51-75% of children have enlarged spleen.
- Holo endemic- where >75% of children have enlarged spleen.

In Holoendemic & Hyperendemic areas there is an intense transmission of P. falciparum & people can sustain >one infectious mosquito bit/day. In such places, morbidity & mortality are considerable during childhood. Immunity against disease is hard one & during adulthood most infections are asymptomatic. This frequent round-year transmission termed stable transmission. In Hypoendemic & Mesoendemic areas the transmission is low, or focal, full protective immunity is not acquired & symptomatic disease may occur at all ages termed unstable transmission.

Characteristics of stable & unstable transmission of malaria.

	Stable	Unstable
Mosquito life	Long	Short
Mosquito bites	Frequent	Rare
Human immunity	High	Low
Epidemics	No (only é rainy Season &migration of non-immunes to the area	Yes
Eradication/contr.	Difficult	Possible

Life cycle



The life cycle of plasmodium is divided into 2, namely:-

1- Asexual cycle: occurs in human, include 2 phases (Liver & Erythrocytic)

2- Sexual cycle: occurs inside anopheles mosquitoes.

Asexual cycle

Liver phase: human infection initiated when sporozoites are injected é saliva during mosquito feeding. The sporozoites enter the circulatory system & within 30-60 minutes will invade a liver cell, undergoes asexual replication. A single sporozoite produces thousands of merozoites (10.000-30.000). This replicative stage called exoerythrocytic (or pre-erythrocytic) schizogony. In P. vivax & ovale some of the sporozoites do not immediately undergo asexual replication, but enter dormant phase known as hypnozoite. This hypnozoite can reactivate & undergo schizogony at a later time resulting in a relapse. The second phase of the asexual cycle is the Erythrocytic phase: in ẃ the swollen liver cells rupture, discharge merozoites into blood stream ẃ then invade RBCs & multiply 6-20 fold every 48-72 hrs. Merozoites recognize specific proteins on the surface of the RBC

& actively invade the cell, after entering the RBC the parasite undergoes a trophic period followed by an asexual replication. The erythrocyte form Ring form due to its morphology in geimsa stained blood smears & as the parasite ⇧ in size this ”ring” morphology disappears & is called trophozoite. During the trophic period the parasite ingests the RBC cytoplasm & breaks down the Hb into amino acids. A by-product of the Hb digestion is the malaria pigment called hemozoin. These golden-brown to black granules of malaria pigment have been long recognized as distinctive feature of blood-stage parasites. The nuclear division marks the end of the trophozoite stage & the beginning of the schizont stage. Erythrocytic schizogony consists of 3-5 rounds of nuclear replication (depending on species), followed by budding process. Late stage schizont in ẃ the individual merozoites become discernable are called segmenters. The host RBC ruptures & releases the merozoites. These merozoites invade ne-w RBCs & initiate another round of schi-zogony. Same cycle repeated invading another RBCs. This explains the anemia in malaria ẃ is largely due to the destrucion of RBCs. When parasites reach certain density in blood, the symptomatic stage begins. During this process the infected RBCs & sometimes uninfected ones are removed from the circulation by the spleen clearance function & contribute its share to anemia. This immunologic function of spleen causes its enlargement. In P. falciparum: the infected RBC containing mature forms adhere to small blood vessels (called cytoadherence) & also é uninfected RBCs forming rosettes (called Rosetting) both of ẃ result in sequesteration of RBCs in vital organs like the brain & heart, interfering é the microcirculation & metabolism & contribute to its severity. This makes detection of mature forms difficult, only ring forms & gametocytes can be

found on peripheral blood films. Sequestration is not a feature of other species of malaria & all stages of the parasite can be seen in the peripheral blood film.

Sexual cycle

After serial of asexual cycles some of the parasites develop into morphologically distinct long lived sexual forms -*microgametocytes*- include male & female, the gametocytes do not cause pathology in the human host & will disappear from the circulation if not taken up by a mosquito that can transmit malaria. After ingestion by the mosquito, the microgametocyte undergoes 3 rounds of nuclear replication, the male & female gametocytes form zygotes, in insect's midgut, this zygotes mature into ookinetes ẃ then develop to oocystes. The oocysts undergo asexual replication (sporogony), ẃ culminates in the production of several thousand of sporozoites. This generally takes 10-28 days depending on species & temperature. Upon maturation the oocyst ruptures & releases the sporozoites ẃ cross the basal lamina into the hemocoel (body cavity of the mosquito). Now it is ready for inoculation to new host.

Clinical picture

The IP is 10-14 days for P. Vivax, Ovale & Falciparum, while it is 18 days - 6 weeks, in case of P. Malaria. The symptoms & signs of malaria resemble many types of febrile illnesses. Early symptoms are nonspecific- malaise, fatigue, headache, muscle pain & abdominal discomfort followed by fever, nausea & vomiting is common. Classically, malaria manifests in regular paroxysms of high grade fever, chills & rigor, occurring every two days in P. Vivax or ovale & every three days in P. Malaria, but it is irregular in P. Falciparum. The malarial febrile paroxysms (ẃ are due to rupture of schizonts & release of pyrogens) typically have 3 stages;

The “cold stage” in ẃ the pt feels intensely cold & has shivering, lasts for 30-60 minutes & characterized by; vasoconstriction of vessels & the temperature ⇧ rapidly. The ”hot stage” pt feels hot, uncomfortable, become delirious, this stage lasts for 2-6 hours. The third & last stage is the “sweating stage” in ẃ the pt will have profuse sweating & exhausted.

Physical findings

Uncomplicated infection: has few physical findings fever, malaise, mild anemia, palpable spleen & liver é mild jaundice (especially children). Suspect in every child é fever **>** 38.5 ^{0}C in endemic areas.

Severe/complicated malaria: defined as life threatening malaria caused by P. Falciparum & the asexual form of the parasite demonstrated in blood film.

Severe/complicated P. Falciparum malaria in adults include:-

- Cerebral malaria: state of unarousable coma lasting for〉30 minutes & other causes of coma ruled out. The change of level of consciousness is less marked than unarousable coma.
- Generalized tonic clonic seizure (〉2/day).
- Severe normocytic anaemia (Hb 〈5 gm/dl).
- ARF (oliguria 〈400 ml/24hr &/or creatinine 〉3 mg/dl).
- Pulm oedema or ARDS. •Hypoglycaemia (BG 〈40mg/dl) is multifactorial (the parasite consumes glucose, the catabolic state ⇧ the glucose demand of the host, anorexia associated é the illness & drugs like Quinine can cause hypoglycaemia).
- Metabolic acidosis (pH〈7.25; plasma bicarbonate 〈15 mmol/l).
- Circulatory collapse, shock, septicaemia: SBP〈80 mmHg.

•Spontaneous bleeding/DIC.

•Haemoglobinuria. •Jaundice, S.B.>3mg/dl.

•Hyperparasitemia: >5% of RBCs affected by plasmodium or >100.000 plasmodium/µl of blood.

•P. Falciparum malaria in pregnant women is also considered as severe because it is associated é adverse outcomes to mother & fetus. The severe complications may occur singly, or more commonly, in combination in the same pt.

People at risk of developing severe malaria in high transmission are:-

- Young Children.
- Pregnant women.
- Visitors to endemic areas.

Types of plasmodium & clinical feature

	Malaria type	I. P.	Fever pattern	Recurrence
Benign	P. Malaria P. Vivax/Ovale	21-42 days 10-21 days	No fever for 2 ay No fever for 1 day	No relapses Relapses possible up to 5 yrs
Malignant	P. Falciparum	10-21 days	Irregular fever	No relapses

Differential Diagnosis

•Trypansomiasis •Relapsing fever •Filariasis •Meningitis •TB •Yellow fever •Typh-oid fever •Brucellosis.

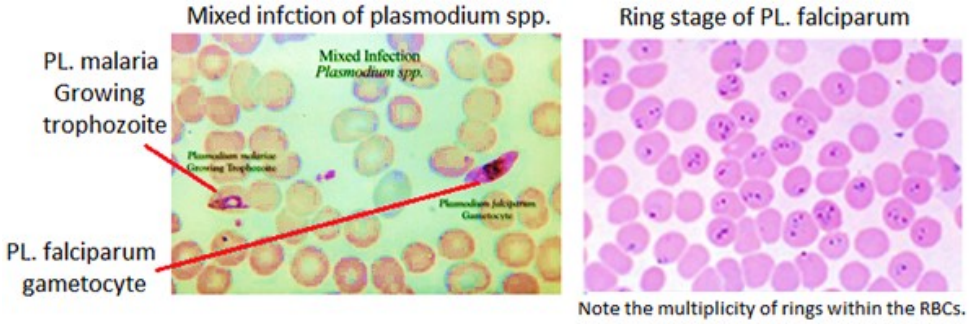
Complications

● Tropical splenomegaly (hyper-reactive malarial splenomegaly) is syndrome from abnormal immunologic response to repeated infection, seen in some residents of malaria endemic area in tropical Africa & Asia, characterized by huge spleen >10 cm BLCM é/éout hepatomegaly. Hypersplenism (anemia, pancytope-

nia), marked ⇧of serum IgM & antimalarial antibody, hepatic sinusoidal lymphocytes, peripheral blood cell lymphocytosis. Splenectomy only indicated for those é failure of antimalarial prophylaxis at least given for 6 months.

●Agranulocytosis ● Rupture spleen ● Hepatitis ● Pigment gall stones ● Black water fever ● Retinal He ● Delirium ● Coma.

Investigations



• ***Demonstration of parasite:*** thin & thick blood film (Giemsa stain):-

Thin blood film is methanol fixed; you can see intact RBC é parasites inside it. Advantage: species identification is simple; % of RBC parasiteized can be estimated.

Thick blood film, not methanol fixed, RBCs are lysed during staining, parasites are seen free from RBC. Its advantage include; concentrates parasite 30 times & this helps to determine parasite conc. N.B. a single blood film examination does not R/O malaria & it should be repeatedly done possibly during febrile episodes. However, studies have shown that blood film can be -ve in small % of pts.

• ***The % of parasite count***: is of prognostic value é Rx, repeat/12 hrs.

• ***Test for sickle cell disease & G6PD deficiency.:*** if proven, ⇩ the dose & prolong the duration of Rx for such proven cases.

• ***Serological studies;*** for detection of antigen: immunochromatography. Detecti-

on of antibodies; indirect florescent antibody assays.

• ***Other tests:*** CBC: anaemia can be detected, RBC appearance, WBCs. CSF when indicated to R/O meningitis. BUN/creatinine, SGOT, SGPT, electrolytes, BG levels.

Treatment

Benign forms of malaria (P. Malariae/Vivax/Ovale)

Chloroquine is effective: the initial dose is 600 mg PO followed by 300 mg after 6, 24 & 48 hrs subsequently, (Chloroquine has no effect on exoerythrocytic liver form &to protect from later recurrences, Chloroquine should be followed by Primaquine 15 mg/day over 2 wks, ẃ is effective against liver forms & gametocytes).

Treatment of P. Falciparum Malaria

a) Aritemisinin & its derivatives: have proved to be highly effective in adults & children. There are different preparations like; Artemether (PO or IM) & Artesunate (PO or IV), Artemether-Lumefantrine: (Coartem or Atmal 20/120): is the most widely used drug, tab containing 20mg Artemether + 120mg Lumefantrine in a fixed dose combin-ation. Adult é < 35 kg BW to be given 3 tab. PO BID for 3 days & for those >35 Kg: 4 tab. PO BID for 3 days. Side effects; dizziness, fatigue, anorexia, nausea, vomiting, abdominal pain, palpitations, myalgia, sleep disorders, arthralgia, headache & rash. These drugs are contraindicated as malaria prophylaxis either alone or in combination, or in case of person é previous history of reaction after using the drug, also contraindicated é pregnant women & mothers é infants <3 months of age & or <5 kg body weight.

b) Quinine: adult dose: 600 mg PO TID for 5-7 days alone or in combination é Tetracycline 500 mg PO QID or Doxycycline 100 mg PO/day for 5-7 days. Side effects: cinchonism: tinnitus, hearing loss,dizziness, tremors,nausea, restlessness,

blurring of vision. Hypoglycaemia: is the commonest adverse effect.

c) Mefloquine: dose is 15mg/kg followed by 2nd dose of 10 mg/kg after 8-12 hrs. Structurally resembles Quinine. The drug is effective against all species of malarial including multidrug resistant P. Falciparum. However some resistance strains of P. Falciparum are reported in some tropical countries.

Side Effects include; nausea, abdominal cramp, vertigo, insomnia, sometimes acute psychosis & convulsion.

d) Sulfadoxine-pyrimethamine (Fansidar): dose is 3 tab. stat as a single dose. (1 tab 500 mg Sulfadoxine + 25 mg Pyrimethamine). Due to high prevalence of resistance to this combination, Fansidar is not recommended for Rx of P. Falciparum in most tropical countries & it is contraindicated for children < one year age.

Treatment of severe & complicated Falciparum Malaria

Pts should be admitted & treated in a hospital setting.

A) Drug treatment

i) Quinine: is the drug of choice for severe & complicated malaria, 20 mg salt/kg by IV infusion over 4 hrs, in 5% Dextrose saline (5-10 ml/kg depending on the pt's overall fluid balance). Maintenance dose: 12 hrs after the start of the loading dose, give 10 mg/kg in Dextrose saline over 4/hrs. Repeat/8 hrs until the pt can take oral medication. Wherever IV administration of Quinine is not possible, give Quinine Dihydrochloride 20 mg salt/Kg loading dose IM divided into 2 sites, in the anterior thigh, then 10 mg salt/kg IM every 8 hrs until pt can swallow.

ii) Artesunate injection: 2.4 mg/kg IV or IM stat followed by 1.2 mg/kg at 12 & 24 hrs & then daily.

B) Supportive treatment

- Bring down fever (cold sponges, paracetamol).
- Administer glucose IV or PO to prevent hypoglycaemia & encourage early PO intake of food.
- Insure adequate fluid intake, check input, output & control water/electrolyte, beware of pulmonary oedema due to fluid overload.
- Consider blood transfusion in severe Falciparum malaria é high parasitemia (**>** 20% of erythrocytes affected by plasmodium).
- Check renal function tests.
- For comatose or unconscious pt proper nursing is mandatory; position pt on his/her sides; turn every 2 hrs to avoid bed sores.
- Catheterize the bladder, monitor input & output, avoid fluid overload.
- Monitor BG regularly & adequate nutrition.

Treatment of Cerebral Malaria/Coma

- Artemether 80 mg amp, starting dose 3.2 mg/Kg IM, then 1.6 mg/Kg daily or Atmal 20/120, 80/240 amp (Artemether + Lumefantrene).
- Dexamethasone, 8 mg /2 ml, 0.5 mg mg /Kg IV/12-24 hrs for 2 days.
- IVF & fluid chart: alternatively use NS, Ringer`s sol & Glucose 5%. Urine catheter.
- Heparin 5000 u/ml/6 hrs.
- Dextran 500 ml over 24 hrs
- Monitor CBC, Malaria indices (% of parasite level 6 hourly).

Prevention

A. General measures

Mechanical barriers

•Draining water collections & swampy areas. •Use of chemical impregnated mosquito nets around beds. •Wire mesh across windows. •Staying indoors at night. •Use of long sleeved shirts/trousers.

Insecticides

•Use insecticide spray aerosols (Permethrin, & Chlorinated Hydrocarbons).

•Insect repellents to exposed skin (e.g. Diethyltoluamide).

•DDT sprayed in the interior of houses is effective in killing the adult mosquito for many months.

B. Drug prophylaxis

In areas where there is Chloroquine resistant P. Falciparum:-

•Mefloquine (resemble Quinin) 250 mg/wk PO, safe during pregnancy.

•Doxycycline 100mg daily orally, not used for children <8 yrs or during pregnancy

•Maloprim (Pyrimethamine + Dapson) 1 tab PO/wk.

•Chloroquine + Proguanil combination.

SCABIES

Scabies is an itchy rash caused by little mite that burrows in the skin surface. The

human scabies mite's scientific name is Sarcoptes Scabiei Var. Hominis, is a common world-wide public health problem é an estimated global prevalence of 300 million. The infestation causes considerable discomfort & can lead to secondary infection & complications such as post-strept glomerulonephritis. The Mites are tiny, just 1/3 mm long, have 8 legs (in contrast to insects, ẃ have 6 legs), not visible é naked eye but can be seen é a magnifying glass or microscope they burrow into the skin to produce intense itching, ẃ tends to be worse at night. A female mite lays eggs under the skin of a human & stays inside until she dies. Mite cannot live> 3 days éout a human host but it can survive up to a month when living on a human. The Mite also lays eggs in human skin that hatch & grow into adult mites. This means that symptoms can last for months or even years.

Transmission

Scabies affects everyone regardless of age, race, gender, social class or personal hygiene habits. Transmission of the mites involves close person-to-person contact of the skin-to-skin variety. It can be transmitted sexually as well as by nonsexual close skin to skin contact especially within family & at school. Almost impossible to get from shaking hands or sitting next to someone. The sexual contact is the most common form of transmission.

Clinical picture

When > one member of household is affected é an intensely pruritic eruption, scabies infestation must be considered. Scabies only affects the skin, causing extreme itching, ẃ is usually worse at night. For the first wks, itching is subtle but gradually becomes more intense until, after a month or two, sleep is almost impossible. Itching may be associated é rashes, blisters, or bumps. Rashes & itching

may last for 2-3 weeks, even after being treated, mainly found in In between the fingers, around the head & neck, wrist, nipple, elbow, waist, armpit, buttocks, penis & shoulder. In children it is especially seen in hands & feet. Text book descriptions of scabies always mention "burrows" or "tunnels“, these are tiny thread-like projections, ranging from 2-15 mm long, ẃ appear as thin gray, brown, or red lines in the affected areas, the burrows can be very difficult to see.

Management

Permethrin 5% cream left on for 8-10 hrs, or 2 applications one wk apart of an aqueous solution to the whole body excluding the head, is usually successful, contraindicated in infants **<** 2 months of age & in pregnancy or lactating mothers. Or 0.5% Aqueous Malathion lotion, left on for 24 hrs. Or Gamma Benzen Hexachlorid 1% lotion. Or Benzyl Benzoate 25% lotion. Sulphur 6% cream daily night application for 3 nights is safe for infants, pregnant & lactating mothers. In some clinical situations such as poor compliance, immunocompromised pt or é heavy infestations (Norwegian scabies), systemic Rx é Ivermectin (200 µg/kg) as a single oral dose would be appropriate. The combination Rx é various topical gent + systemic agent in AIDS & immunocompromised pt ensure eradication.

YELLOW FEVER

Viral hemorrhagic fever, transmitted to man form monkeys through female mosquito Aedes Egypti, This female Aedes egypti mosquito is a known transmitter of dengue fever & yellow fever & lastly Zeka virus (in South America) ẃ cause microcephaly & incomplete brain development. The Zika virus was first discovered in the 1940s, though most people had never heard of it until this year. That's because for decades, Zika outbreaks were sporadic and tiny & the disease seemed to do little harm. The Yellow fever was diagnosed in 1648. The disease occurs now only in Africa, Central & South America. A Egypti is sometimes referred to as the yellow fever mosquito. The viruses are transferred to the host when man has been bitten by a female mosquito. IP 3 -6 days, Hge result from affection of liver & ⇩ of all clotting factors, progress to DIC & death rate is 3%.

Clinical Picture

- Mild cases: high fever, ⇩ HR, Headache, back pain, chills & muscle aches.
- Second phase: jaundice, hepatosplenomegaly, hepatic necrosis, bleeding from nose, epistaxis & hematemesis (black vomit).

Investigations

- CBC: leucopenia, thrombocytopenia.
- ELISA test, PCR: for detection of antibodies to virus, & for follow up.
- Liver function tests.

Management

Supportive treatment: including:-

- IVF & Plasma.
- Peritoneal dialysis may be needed.
- Prophylactic vaccination.

EBOLA HEMORRHAGIC FEVER

Epidemiology: the deadly African virus, >20 previous Ebola & Marburg virus outbreaks. 2014 West Africa Ebola outbreak caused by *Zaire Ebola virus* species (five known Ebola virus species). Early diagnosis is rare, condition mimic malaria, marburg disease, typhoid. IP 2 days - 3 weeks, transmitted from wild animals to man through monkeys, fruit bats, pigs. Spread as epidemic from man to man through direct contact é blood, body fluids, air born, droplet infection from cough. When WBCs attack the EBOLA virus, the WBCs dissolve liberating chemicals in blood ẃ in return stimulate the release of other chemicals in blood as cytokines, procoagulase, anticoagulants, causing permanent bleeding ẃ is characteristic feature.

Clinical picture

- Day 7-9: headache, fatigue, fever, muscle soreness.
- Day 10: sudden high fever, haematemesis, passive behaviour.
- Day 11: brusing, brain damage, epistaxis, bleeding from nose, mouth, eyes.
- Day 12: loss of consciousness, seizures, massive internal bleeding, & death.

Ebola is associated é impairment of LFTs & RFTs, maculopapular rash, echymosis, purpura, hematoma, especially around needle injection site in about 50% of cases, DIC, bleeding represent very poor prognosis associated é focal tissue necrosis of kidney & liver.

Investigations

*__CBC:__ leukopenia followed by neutrophilia, platelets ⇩ (50,000-100,000/ml).

*__Coagulation profile:__ prolonged PT & PTT.

*__LFTs:__ ⇧ SGOT & SGPT.

*__RFTs:__ proteinuria, ⇧ creatinine. *__Electrolyte__ abnormalities from fluid shifts.

*__RT-PCR:__ used for diagnose of acute infection.

*__Virus isolation:__ requires biosafety level 4 laboratory, can take several days.

*__Serologic testing:__ for IgM & IgG antibodies (ELISA) for detection of viral antibodies in specimens, blood, serum, or tissue.

*__Monitoring:__ of the immune response in confirmed Ebola pts.

Management

✶No specific Rx, no vaccination available & the mortality rate is 90%.

✶IVFs. Some try to use blood transfusion?

✶Complete precautions for medical staff, wearing several layers of protective clothes covering the entire body, masks, gloves.

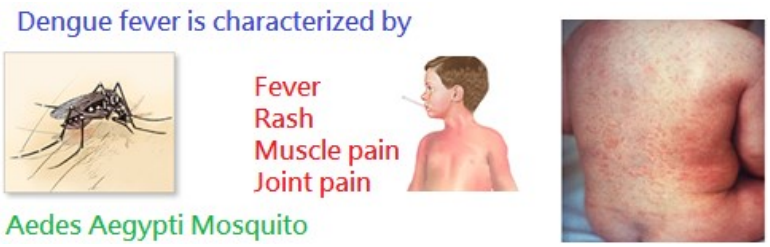
✶Proper disposal of excretions.

✶ Proper disposal of victims bodies after death.

✶Disinfectant of homes of dead or infected persons.

✶Stop contact é infected animals & consumption of their meat.

DENGUE FEVER



Epidemiology: Dengue in recent yrs has become major international public health concern. Dengue is found in tropical & subtropical regions around the world, predominantly in urban & semiurban areas. Was 1st recognized in the 1950s during the dengue epidemics in the Philippines & Thailand, but today DHF affects most of Asian countries & has become a leading cause of hospitalization & death among children. The disease is now endemic in >100 countries in Africa, Americas, Eastern Mediterranean, Southeast Asia & the Western Pacific. WHO currently estimates there may be 50 million cases of dengue infection worldwide every year.

Vector: Aedes aegypti & Aedes albopictus.

Clinical Picture

- Fever: continuous for 3 to 5 days.
- Severe headache.
- Painful limbs, joints, back muscles, pain behind eye ball.
- Rash appears on the 3rd - 4th day after onset
- Nausea, vomiting.
- Slight gum bleeding & nasal bleeding.
- Extreme fatigue & depression may follow recovery.
- In very rare cases, the condition may worsen into DHF, leading to Hge, shock or even death. DHF include 4 grades:-

*Grade 1: Fever & nonspecific constitutional symptoms.

*Grade 2: grade 1 manifestations + spontaneous bleeding.

*Grade 3: signs of circulatory failure (rapid/weak pulse, narrow pulse pressure, hypotension, cold/clammy skin).

*Grade 4: profound shock (undetectable pulse & BP).

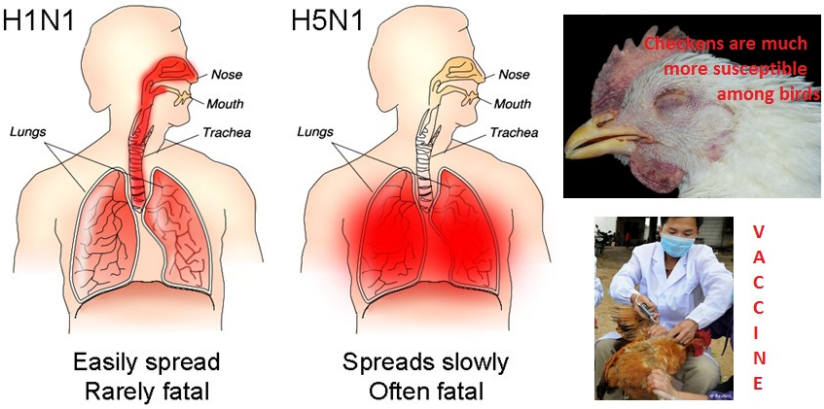
Investigations

- ***Isolation of the virus.***
- ***⇧ IgG or IgM antibodies titres.***
- ***Antigen detection:*** immunohistochemistry, immunofluroscence, ELISA. PCR.
- ***CBC:*** leucopenia & thrompocytopenia.

Management

At present, there is no specific Rx, pts é classical dengue usually rec- overs in 1 to 2 wks. For serious cases, supportive Rx is provided by hospitals. No aspirin because they worsen the Hge, no pain killers, no antibiotics are of proven value, no steroids. Plenty of water & salt are required. Paracetamol for fever.

AVIAN INFLUENZA



Avian influenza virus of the genus Influenza virus A, Family Orthomy-xoviridae. Classified into many subtypes based on the surface antigens “Hemagglutinin” ẃ include 16 types & Neuraminidase 9 types. The high pathogenicity avian influenza (HPAI), causes severe disease in poultry. The low pathogenicity avian influenza (LPAI) cause mild disease in poultry, The LPAI can mutate into HPAI.

Reservoirs: waterfowl & shorebirds

Incubation period: difficult to determine- 2-17 days possible

Clinical picture: H5N1 infections in humans cause; high fever, upper respiratory symptoms, mucosal bleeding, gastrointestinal symptoms & pt may deteriorate rapidly. The late symptoms include; organ failure, DIC.

Communicability: rare cases of person-to-person transmission. No cases of sustai-ned transmission. Faecal shedding & transplacental transmission are ?

Diagnosis: PCR, Primary test to identify H5N1, Antigen detection, Virus isolation

Management: Antiviral drugs; Amantadine, Rimantadine, Zanamivir, Oseltamivir. Currently circulating H5N1 viruses may be resistant to Amantadine & Rimantadin.

Protection of humans: avoidanance of contact é poultry, food safety inspection service, proper food handling & preparation & bird vaccination.

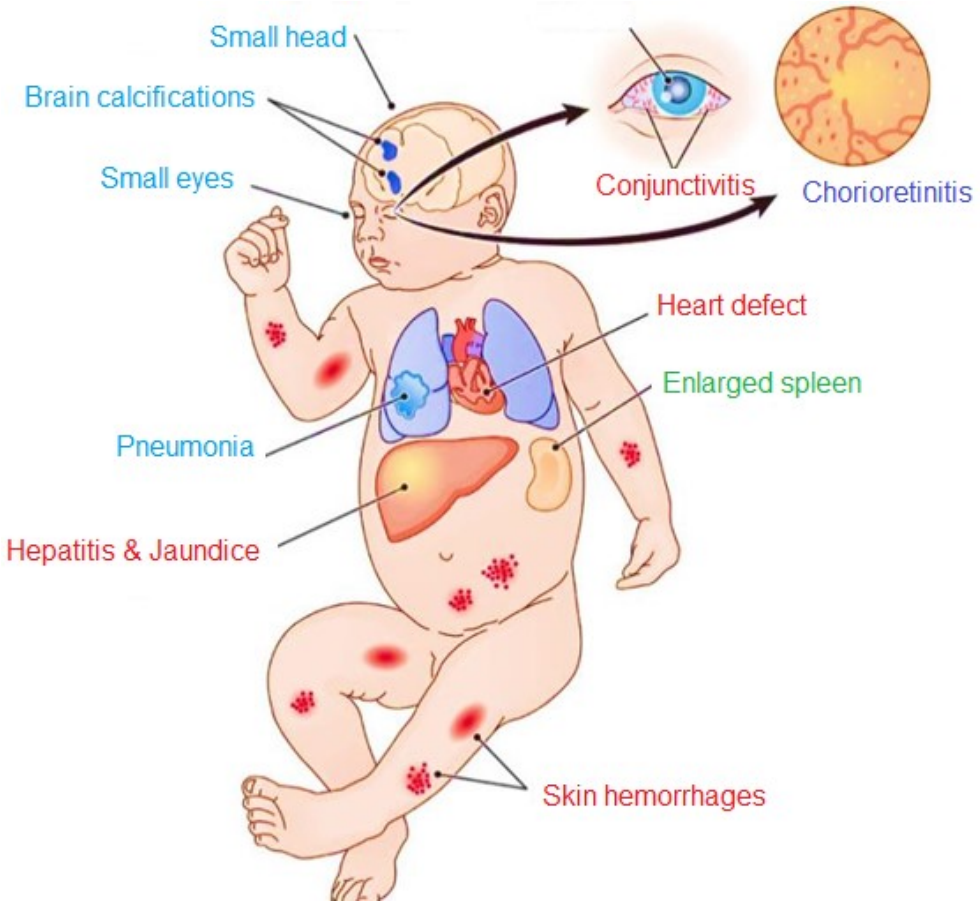
PYREXIA OF UNKNOWN ORIGIN

Fever ẃ lasts for > 2 wks ēout reaching a clinical or laboratory diagnosis. If fever is more by night you can think in TB, typhoid or brucellosis. If fever is associated ē bradycardia, think in typhoid or yellow fever.

Investigations

- CBC: may show Leukemia, or marked ⇧ of eosinophilic count in case of parasite infect.
- Antibodies: for parasitic infestation as; Fasciola Hepaticus, Bilharziasis, Amoebiasis, Toxocariasis, Hydated, Toxoplasmosis, Leishmaniasis, Trichenella.
- Antinuclear antibodies: for juvenile Rh^{ed} arthritis.
- Double strand DNA: for SLE.
- Blood film: for malaria.
- U/S abdomen: for liver abscess, abscess, tumors as neuroblastoma.
- Urine catecholamine VMA, HVA: for neuroblastoma.
- CXR: for lung abscess.

INTRA UTERINE INFECTION

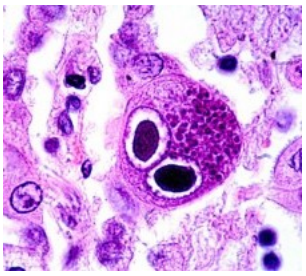


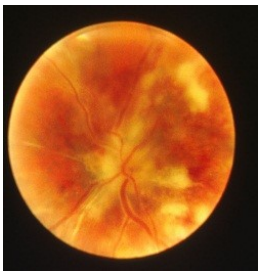
Is major cause of PT labor, represent an approximately 25% of all PT births. The earlier the gestational age at delivery, the higher the frequency of IUI. It is considered as one of the major maternal insults during pregnancy. The incidence of IUI during pregnancy is estimated to be about 14% when laboratory methods of detection are used. The commonest IUI are; toxoplasmosis, rubella, syphilis, CMV, herpes simplex, hepatitis B, HIV (TORSCH) & others include; Coxsackie, Varicilla zoster, Parvo viruses.

Preventive measures

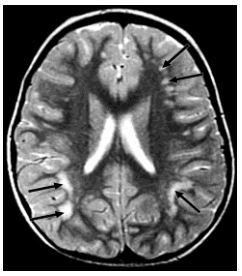
Are necessary since lesions caused by some IUI are permanent & damaging. TORCH`S screening for every pregnant women is a medical acronym for a set of perinatal infection transmitted from the mother transplacentaly or during labor.

CONGENITAL CYTOMEGALO VIRUS INFECTION


Cytomegalo cells


Chorioretinitis


Deafness


Cerebral calcification

In 1920, Good Pasture correctly postulated the viral etiology of the histopathological changes, probably in tissues from a congenitally infected infant & he used the term cytomegalia to refer to the enlarged, swollen nature of the infected cells, the virus was first isolated in 1956, it is 1 of 8 human herpes viruses. The incidence of congenital CMV infection varies widely throughout the world ranges from 0.2-2.2% of live births. It is considered one of the most serious infections during pregnancy. There is significant risk increase of adverse fetal effects if infection occurs during the first half of pregnancy. It was estimated that 50-80% of adults in USA have had a CMV infection by the age 40 yrs, it is one of the STDs & once CMV is in a person`s body, it stays there for life. Infection acquired to the baby either transplacentaly, or during labor through contact é infected cervical secretions, or during breast feeding & through contaminated blood transfusion.

Clinical picture

The Mother: usually have no symptoms, or mild manifestations of flu like as fever, mu-scle ache, headache, but infection can be very serious in people who have received organ transplants or immunocompromised people.

The Baby: is asymptomatic; in 90% of cases, infant appear healthy at birth, but 10-15% of those babies may develop late squeals, especially hearing defects after a period of months or even years.

Symptomatic baby; in 5% of cases, severe fetal damage & in rare cases death due to abortion, or é manifestations of; SGA, hepatosplenomegaly, petechiae (purple skin splotches or rash or both), thrombocytopenia, prolonged NN jaundice, pneumonitis, microcephaly, occasionally cerebral calcification, later complication include; CP, epilepsy, MR, visual impairment, chorioretinitis, optic atrophy, delayed psychomotor development, expressive language delay, learning disabilities & deafness.

Diagnosis

*Culture from body fluids, or tissue biopsy specimen (blood, saliva, throat swab, CSF, urine, stool, vaginal secretions, breast milk, semen of father), culture monitored for development of CMV-associated cytopathic effect.

*PCR.

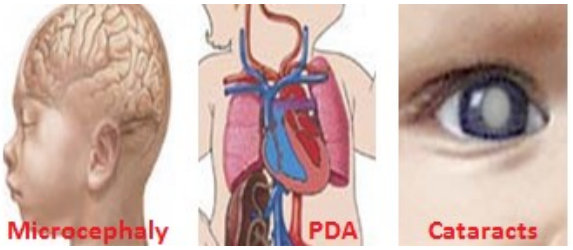
*CMV IgM.

*ELISA (Enzyme Linked Immune Sorbent Assay) test is diagnostic.

Treatment

No specific treatment, there is some evidence that Ganciclovir (500 mg amp) -antiviral- may prevent hearing loss & developmental outcome in infants born é symptomatic CMV infection, the dose from age 6 months -16 years is equal to 5 mg/kg/12 hours IV for 7-14 days, or PO (250 mg cap) 15 mg/Kg twice daily & one of its main side effects is bone mar-row suppression.

CONGENITAL RUBELLA SYNDROME



The name Rubella is derived from a Latin term meaning“Little Red”, was 1st described in 1941 by Australian Ophthalmologist Norman Gregg, who had noticed an unusual number of infants é cataracts following rubella epidemic in 1940. In 1964–1965 worldwide outbreak occur result in an estimated 12.5 million cases & 20.000 cases of congenital rubella syndrome (CRS) & 2100 NNDs of CRS in USA only. The virus was isolated in 1961 & vaccine developed in 1969, this is the shortest time period from virus identification to vaccine ever. The introduction of the MMR vaccine & screening program for pregnant mothers improve dramatically the incidence of CRS in countries applying this system. Worldwide it was estimated that >100.000 infants born é CRS annually, as it is still common in many developing countries. The infection caused by rubella virus ẃ is a member of the rubivirus group, it`s IP is 2-3 weeks & there is 90% chance of passing infection transplacentaly if mother get infected during the 1st TM, but fetal damage is rare after 12 weeks gestation.

Clinical Picture

Sensorineural deafness (in 80% of cases). MR (55% of cases), Cataract, Retinopathy, Micro-ophthalmia (50% of cases). PDA- (50% of cases). Meningoencephalitis (25% of cases). DM type1 (20% of cases). LBW. SGA. Hepatosplenomegaly. Generalized lymphadenopathy. NN jaundice. Thrombocytopenia. Abnormal skull. Microcephaly. Microganthia. IC calcification. Schizophrenia & Autism.

Diagnosis

Mother: detection of IgM Rubella specific in mother saliva sample, or maternal blood is both sensitive & specific, indicates primary infection & ⇧ in IgG titer over 2 weeks usually occurs.

Baby: isolation of rubella virus from blood, nose, throat, or urine. Detection of IgM rubella specific & PCR +ve for rubella virus.

Management

Pregnancy termination if rubella specific IgM is +ve in the 1st 16 wks. Screening programme used in many western countries for all adolescent girls in their 2ry school to detect rubella antibodies & if -ve, the girl must be given MMR vaccine.

CONGENITAL HERPES SIMPLEX

NN infection é HSV was 1st reported in 1935 by Dr. Hiss M. who reported a case of hepatoadrenal necrosis é intranuclear inclusion bodies. It is one of the STDs, infection also can transmitted through skin to skin contact. The NN infection, mostly caused by type 1 HSV, while 25% caused by type 2 HSV, the risk is more higher if the 1st attack (painful & itchy) occur after the 28th week of pregnancy.

85% of transmission occur during birth when a baby come in contact é infected genital secretion in the birth canal. 5% occur through transplacentaly. 10% acquired the infect-ion postnataly. The incidence of congenital Herpes 1/3000-20000 live births in USA.

Clinical picture

Mortality rate in NN is 100%, the diagnosis can be difficult, but should be suspected in NN when one of parent have positive history of herpes infection, or pregnant mother é itching, discharge, vesicles in vulva, lower abdominal pain, inguinal lymphadenopathy, or in case of baby é irritability, lethargy, fever, poor feeding at the 1st week of life. The baby infection is either:-

*Localized Skin, Eye, Mouth: the skin lesions appear as small, fluid filled vesicles, these vesicles rupture, crust over & finally heal, often leaving a mild scar.

*Encephalitis: presented é seizures, tremors, lethargy, irritability, poor feeding & bulging fontanels.

*Disseminated form: is another presentation involving the CNS, lung, liver, adrenals, SEM. The transplacental transmission may presented é micro or hydrocephalus, chorioretinitis & IC calcification.

Diagnosis

*Isolation of the virus by culture from; blood, CSF, oropharynx, urine, stool, skin vesicles, eye or nose secretions.

*Positive PCR for HSV.

*ELISA test for HIV.

Management: it has been recommended that CS should be performed if acute lesions are present at the onset of labor.

Mother: é proven HSV infection in the late 3rd TM, or mother é active recurrent genital herpes, oral Acyclovir 400 mg tid from 36th wk of gestation until delivery & breast fee-ding is allowed, as the HSV not transmitted through breast milk.

Baby: é proven HSV infection, IV Acyclovir 60mg/kg/D ÷3 equal doses for 2-3wks.

CONGENITAL HEPATITIS B

The WHO has estimated >350 million people over the world are chronically infected é HBV. In adults, infection transmitted through; drug abuse, high risk sexual activities, multiple sexual partner, sexual partner é viral hepatitis, infected blood or blood product transfusion, infected needle & tattoos. The IP of the disease may vary from 6 wks up to 6 months. If pregnant woman is a HBV carrier é HBeAg +ve, her NN has a 90% likelihood to be infected & become a carrier. 25% of those babies will die later during adulthood from chronic liver disease or liver cancer. The availability & extensive use of HBV vaccine has dramatically ⇩ the number of incident infections in many countries. The HBV, is large virus & does not cross the placenta, hence it can`t infect the fetus unless there have been breaks in the maternal fetal barrier, most of cong. HBV infection (90-95%) occur during delivery from abrasions in the infant`s skin or mucosa or from small maternofetal bleeds across the placenta during labor, while transplacental transmission occur in 5%. The mode of delivery does not influence the vertical transmission. Hepatitis B is the only STD to have protective vaccine.

Clinical picture

Almost all infections in the neonates are asymptomatic but >90% become chronic carri- ers & at high risk for chronic liver disease, cirrhosis & hepatocellu- lar carcinoma during adulthood compared é only 5-10% of individuals acquiring HBV infection as adolescents or adults.

Risk factors for HBV transmission

Maternal HBeAg +ve, high maternal HBV DNA, threatened preterm labor & threatened abortion.

Investigations

Mother: acute HB or persistent carrier state, will show; +ve HBsAg, +ve HBe Ag & +ve anti HBc (IgM or IgG).

HBs Ag: is the surface antigen of hepatitis B virus, it indicates current HB infection, commonly referred to as the Australian antigen, this is because it was first isolated by the American research physician & Nobel prize winner, Baruch Blumberg in the serum of Australian person, it was discovered to be part of the virus that cause hepatitis by virologist Alfred Prince in 1968.

HBeAg: appear during 3-6 wk of infection & it indicate that pt is infectious & its persistence >10 wk indicates chronic infection.

HBc Ag: not detectable in blood but in liver cells (biopsy).

anti HBc IgM: denotes early acute infection.

anti HBc IgG indicate chronic infection.

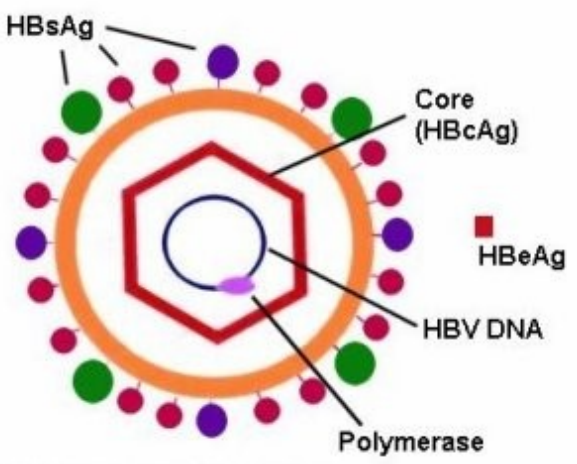
anti HBe: prognostic for resolution of infection.

anti HBs: indicate clinical recovery & subsequent immunity.

Disease stage	Serological markers
Acute disease	HBsAg , antiHBc IgM
Chronic disease	HBsAg
Infectivity	HBsAg , HBeAg , Viral DNA
Recovery	antiHBe, antiHBs
Carrier state	HBsAg* , antiHBc (total)
Immunity	antiHBs , antiHBc (total)
Past immunization	AntiHBs

**Persisting for more than 6 months*

Infant: +ve HBsAg is indicative of acute infection & it`s persistence for >6 months is indicative of chronic infection.



Management

Mother: screening of all pregnancies for HBsAg, if pregnant women is +ve she should be given hepatitis B immunoglobulin. No antiviral agent has been approved for use during pregnancy, "the risk-benefit equation of using antiviral depends upon age of mother, the trimester of pregnancy & her stage of liver disease".

Baby: should be given HB hyper immunoglobulin at birth, followed by HBV vaccination, the first dose to be given within 12 hours of birth, second dose at 1 month age & third dose at 6 months age, this regime is 95% effective in prevention of HBV perinatal transmission. Heptavax, is the 1st generation of hepatitis B vaccine in 1980`s was made from HBsAg extracted from the plasma of HB pts. Current vaccine is made from recombinant HBsAg in grown yeast. Breast feeding by HBsAg +ve mother is not known to ⇧ the risk of transmission & therefore not contraindicated.

CONGENITAL SYPHILIS

Snuffles  Desquamation  Periostitis 

Syphilis is a STD, has been recognized since antiquity, in infancy it was described as early as 1497 & the causative microbe Treponima Palladium, was discovered in 1905, congenital syphilis still serious, under diagnosed & is a threat for children in poor countries. WHO estimate that there were 2 million syphilis infections among pregnant women annually. In 2007, WHO, launched an initiative to eliminate syphilis, that set targets of at least 90% of pregnant women being tested for syphilis & at least 90% of sero positive pregnant women to receive adequate Rx by 2015. Congenital syphilis is caused by passage of bacteria from mother to the child during fetal development especially before 16th week of gestation or at birth. Untreated syphilis results in a high risk of a poor outcome pregnancy e.g. miscarriage, preterm labor, IUGR, stillbirth. Some infants é congenital syphilis have symptoms at birth, but most develop symptoms later.

Clinical picture

Early signs of cong syphilis

Those appearing in the first 2 years of life are in the form of;

*Bone lesions: osteochondritis, periostitis, pseudo paralysis (secondary to pain or fracture) affecting long bones, cranium, ribs, spine…….. (78% of cases)

*Hepatosplenomegaly, jaundice, lymphadenopathy…….. (71%)

*Skin lesions: extremely variable; macular, vesicobullous, bullous (pemphigus syphili- ticus), desquamation (washer woman skin palms, soles), rash in mouth or

genital area, paronychia, mucous patch, condylemata lata…….(68%)

*Fever …… (42%).

*Failure to thrive……..(33%)

*CNS involvement: leptomeningitis, seizures, hydrocephaly……..(23%)

*Pneumonitis……..(17%)

*Snuffles……(14%)

sero sanguineous discharge from nose, saddle shaped nose (collapse of the bony part of nose).

*Chorioretinitis, uveitis & glaucoma.

The late signs of cong. syphilis: appearing later over the first 2 decades of life include; *Hutchinson`s teeth (centrally notched, widely spaced shaped upper central incisors).

*The triad of Hutchinson teeth, keratitis & deafness occur in 63% of cases).

*Rhagades: linear scar at the angles of mouth & nose é secondary infection.

*Skin scaring around the mouth, genitals & anus.

Investigations: •Detection of Trep. Palladium (in blood or secretions). •FTA-ABS Flourescent Treponema Antibodies Absrption Test. •PCR. •VDRL. •CSF •Bone XR.

Management

Aqueous Crystalline Penicillin G 100.000-150.000 u/kg/day IV divided into 2 doses for 10 days, or Procaine Penicillin G 50.000 u/kg/day IM as a single daily dose for 10 days. In case of allergy, children should be desensitized.

Desensitization technique

① 0.1 ml 1/20 conc + 0.05 ml adrenaline SC watching for local or systemic raction

② 0.1 ml 1/10 conc + 0.05 ml adrenaline SC after 30 min.

③ 0.01 ml full conc + 0.05 ml adrenaline SC after 30 min.

④ 0.1 ml full conc + 0.05 ml adrenaline SC after 30 min.

⑤ 0.5 ml full conc + 0.05 ml adrenaline S.C after 30 min.

⑥ Full dose IM after 30 min. é the presence of adrenaline & forticort ready to use.

CONGENITAL HUMAN IMMUNE DEFICIENCY VIRUS

STD, worldwide there were 2.5 million new cases in 2011 & about 34.2 million people are living é HIV around the world, once a person is infected, the virus remains in the body for life, there is no cure for AIDS but there are drugs that help control the virus, enabling people to live a full & healthy lives. HIV may be transmitted from mother to baby at any time during pregnancy, or labor in 65% of cases, or as a result of breast feeding. HIV infection progressing to AIDS over 8-10 years.

Factors ⇧ the risk of transmission

•Acute stage of mother illness. •High maternal viral load. •Low maternal CD4 count. •PRM or premature delivery. •Abruptio placenta. •Vaginal delivery. •Breast feeding.

Clinical picture

Recurrent bacterial, fungal, or viral infection, wasting, delayed milestones.

Investigations

During pregnancy, the fetus passively acquires maternal HIV antibodies across the placenta, this does not mean the fetus is infected, it can take up to 12-18 months for a baby to clear these maternal antibodies. PCR test is very accurate & the best test to diagnose HIV infection in babies, by detection of HIV-DNA-PCR

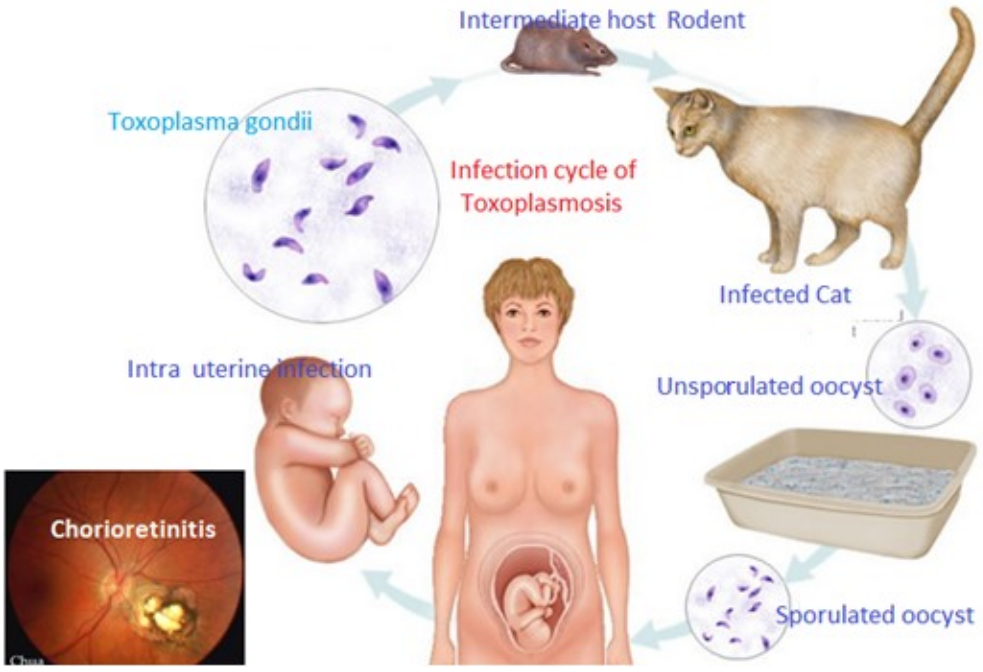
(qualitative) or HIV-RNA-PCR (quantitative) ẃ is more valuable. A positive PCR test must be confirmed by repeat test to confirm infection. CD4 cells sometimes called T cells, are a type of lymphocyte, they are an important part of the immune system. When HIV infects humans, the cells it infects most often are CD4 & when someone is infected for a long time, the number of CD4 they have drop dramatically (normal value of CD4 cells is 500-1600/ml^3 blood = 20-40%) & any one é CD4 < 200 (< 14%) is considered to have serious immune damage. The T lymphocyte cells (CD4) stimulate the production of interleukin 2 ŵ in turn stimulate the production of T-killer & T suppressor cells, both act to regulate the defensive mechanism against infection, also T lymphocyte stimulate the production of B lymphocytes & plasma cells ŵ in turn stimulate the production of complement (neutralization of bacteria), opsonin (opsonization of bacteria) & immunoglobulin, all responsible for cellular & humoral immunity in the body.

Management

Pregnant mother: HIV treatment is life long, if pregnant mother proved to have HIV infection or her CD4 count < 500, antiretroviral drug therapy, Zidovudine "ZDV" 250 mg PO twice daily or Azidothymdine "AZT" after the 14^{th} week of gestation & to continue throughout pregnancy in addition to intrapartum intravenous ZDV (amp 20 ml = 200 mg), starting 4 hours prior to CS, at a loading dose of 2 mg/kg over one hour then 1 mg/kg hourly until the umbilical cord is clamped. HIV may become resistant to ZDV or AZT over time & for this reason it may be used in conjunction é other anti HIV drugs, called Highly Active Anti-Retroviral Therapy (HAART) include; Efavirenz +Tenofaver + Emtricitabine, given according to certain protocol & follow up schedule for CD4 & PCR.

Baby: if pregnant mother proved to have HIV infection, baby must be given Zidovudine syrup (5 ml contain 50 mg), starting 8 hours after birth in a dose of 2 mg/kg/6 hours for 6 weeks, if baby is PT or unable to tolerate feeds, IV infusion used & the baby is closely monitored by PCR monthly for the first 4 months, then PCR & CD4 every 3-4 months until age of 18 months to completely R/O HIV infection. Prophylactic for pneumocystis carinii pneumonia, Cotrimoxazole syrup 0.5 ml/kg/day should be initiated when infants are 6 weeks old & continued for at least 4 months. No BCG or live vaccines should be given.

CONGENITAL TOXOPLASMOSIS



Caused by infection é the protozoan parasite, 1st identified & isolated from African rodent in 1908 by Drs Niclle & Manceaux. In 1909 the parasite was named Toxoplasma Gondii. In 1923 Janku reported parasite cysts in the retina of an infant who had hydrocephalus, seizures & bilateral micro ophthalmia, while the first adult infection was recorded in 1940. Human infection may be acquired by ingestion of oocyte excreted by cats&contaminating soil or water, or by eating

tissue cysts that remain viable in undercooked meat of infected animals. There are considerable geographic differences in prevalence rates. The sero +ve (IgG) women in the childbearing period is about 50-80% in Latin America & 30-50% in Middle East. It's rare that a women who got toxoplasmosis before getting pregnant will pass the infection on to her baby, but if she catch it during pregnancy & remain untreated there`s a chance that she could pass infection on to her developing fetus & Babies who become infected during their mother`s first trimester tend to have the most severe symptoms. Infection in adult are usually either asymptomatic or associated é self-limited symptoms as fever, malaise & lymphadenopathy.

Clinical picture

90% of babies born é cong toxoplasmosis have no symptoms early in infancy, but large % of them will show signs of infection months or years later. include;

- Prematurity.
- Persistent jaundice, hepatosplenomegaly, anemia.
- MR.
- Hydrocephaly or microcephaly.
- Intracranial calcification, chorioretinitis, blindness, epilepsy
- Skin rash (tiny red spots/petechiae).

Investigations

Pregnant women: +ve toxoplasma specific IgM & IgG indicate recent infection but +ve toxoplasma specific IgG only indicate old infection ŵ leads to a lifelong antibody.

Infant: toxoplasma antibodies (IgG) are passed from the mother to the baby thr-

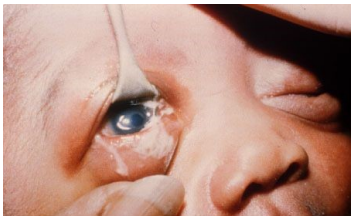
ough the placenta & could be of maternal origin, while +ve toxoplasma specific IgM (can`t pass the placenta) indicates infected baby.

Management

Pregnant women: é confirmed infection, Pyrimethamine: loading dose 100mg/ day divided into 2 doses for 2 days & the maintenance dose is 50 mg/ daily.

Infant: Pyrimethamine: loading dose 2 mg/kg/day for 2 days, then 1 mg/kg/day for 2-6 month, maintenance every Monday, Wednesday & Friday for 1 year + Sulphadiazine 100 mg/kg/day ÷ 2 doses for one year + Folic acid 10 mg/ 3 times weekly for one year.

NEONATAL CONJUNCTIVITIS



Conjunctivitis in general include the following causes:-

*Chemical: occurs in the 1st day of life, result from conjunctival irritation by blood or meconium during labor.

*Gonococcal: manifest in the 2nd-3rd day of life, the conjunctival discharge is purulent (ophthalmia neonatorum). Diagnosed by culture of the baby conjunctival discharge, swab from mother urethra, cervix & vagina. Condition treated by; Penicillin 6 hourly, Mephenicol eye drops ½ hourly for 6 hours, then 4 hourly 5 days, Mephenicol ointment twice daily (in addition to treatment of the mother).

*Chlamydia infection: occur in the fifth day of life, associated é severe congestion (Erythromycin is effective treatment).

*Viral: characterized by severe congestion, subconjunctival He, it takes about 1-2

weeks to subside, symptomatic treatment (Visine, Tresolin, Dexapolyspectran eye drops).

Clinical Finding	Bacterial	Viral	Allergic
Bilateral eyes	50% to 74%	35%	Mostly
Discharge	Mucopurulent in younger children	Mild, watery, or "sleepers" only	Rare
Redness	Common in older children, uncommon in infants and toddlers	Usually	Usually
Acute otitis media	32% to 39%	10%	No
Pruritic	No (but many rub eyes)	No	Major